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Titanacyclobutene Complex Formation *via* Inter- and Intramolecular Radical Reactions. Nitrile Insertion Reactions of Titanacyclobutene Complexes.

by

Paul Byron Tiege

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Doctor of Philosophy

Department of Chemistry

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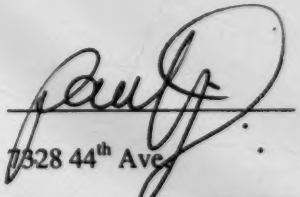

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research for acceptance, a thesis entitled: **Titanacyclobutene Complex Formation *via* Regioselective Inter– and Intramolecular Radical Reactions. Nitrile Insertion Reactions of Some Titanacyclobutene Complexes, and Conversion to Tetra–substituted Pyridines**; submitted by Paul Byron Tiege in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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Abstract

This thesis describes an investigation into the formation and functionalization of titanacyclobutene complexes arising from free radical alkylation of titanium(III) propargyl compounds from three titanium(III) starting materials; Cp_2TiCl, $(^tBuCp)_2TiCl$, Cp^*_2TiCl. It continues and complements the work completed and in progress at the time especially with respect to small, medium, and large ring synthesis by intramolecular free radical cyclization reactions. In particular, the upper limits of ring size formation were probed in the Cp, ^{t}BuCp, and Cp* ancillary ligand series with the simple α,ω-dibromo-2-yne substrates. Bicyclic compounds with appended allene functionality were constructed by use of an α,ω-bispropargyl class of substrates. The syntheses of both classes of substrates is described. As well, the use of vinyl radicals to alkylate the titanium propargyl π–complex to form titanacyclobutene complexes with conjugated diene moieties is described. The investigation also demonstrates that the radical addition to the propargyl substrates is facilitated by the more electron-donating ligand sets: titanacyclobutene complex yields decrease in the order Cp*, ^{t}BuCp, Cp. Additionally, ring sizes that are attainable are also dependent on the ancillary ligand set with the largest sizes accessible from the Cp* series. The functionalization of titanacyclobutene complexes by reaction with nitriles is described, as is the transformation of some of the nitrile insertion products into pyridines. Some preliminary work on the transmetallation of titanacyclobutene complexes to boron and phosphorous is presented.

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to my parents

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List of Abbreviations

Å	angstrom
Ac	acetate
AIBN	2,2'–azobisisobutyronitrile
Bn	benzyl
Bu	butyl
^{t}Bu	tert–butyl
calcd.	calculated
Cp	cyclopentadienyl
Cp*	pentamethylcyclopentadienyl
cy	cyclohexyl
COSY	correlated spectroscopy
DMPU	N,N'–dimethylpropylene urea
EHMO	extended Hückel molecular orbital
et	ethyl
eq	equivalent
FMO	frontier molecular orbital
g	grams
h	hour(s)
HMQC	heteronuclear multiple quantum correlation
HMBC	heteronuclear multiple bond correlation
HSQC	heteronuclear single quantum correlation
HMPA	hexamethylphosphoramide
Hz	Hertz
HOMO	highest occupied molecular orbital
i	iso
IR	infrared
L	litre
LUMO	lowest unoccupied molecular orbital
M	metal

Me	methyl
MeCN	acetonitrile
mL	millilitre
MS	mass spectrometry
MsCl	methanesulfonyl chloride
NMR	nuclear magnetic resonance
Ph	phenyl
^{i}Pr	isopropyl
R	alkyl group
SBR	samarium Barbier reaction
SGR	samarium Grignard reaction
SOMO	singly occupied molecular orbital
t	tert
THF	tetrahydrofuran
THP	tetrahydropyran
tlc	thin layer chromatogram
TMS	trimethylsilyl
tol	toluene
TsCl	toluenesulfonyl chloride
Tr	triphenylmethyl
η	hapticity
μL	microlitre

Chapter 1. *Introduction and Historical Perspective.*

A radical reaction is a chemical process in which molecules having unpaired electrons are involved. The number of odd–electron processes reported in both the organometallic[1,2] and organic chemistry[3,4] literature has increased substantively in the last two decades, heralding a new era in carbon–carbon bond formation. The inherent dynamics of radical processes, which have made radical chemistry somewhat pariah to mainstream organic synthesis for so long, have been exploited to reveal tremendous, previously unattainable, reactions and reactivities that can be executed precisely and in controlled fashion.[5]

The use of organometallic compounds has increased the scope of this field. The nascent science of transition metal–promoted free radical reactions exhibits a number of advantages over other radical strategies. These reactions can show unique selectivity and reactivity patterns because the metal centre can be electronically and sterically fine–tuned to optimize reactivity and compatibility with the radical reactions they promote. The electron density on a specific metal centre can be used to control the reactivity of that metal. The electronic profile can be modulated by varying the ligands around the metal. Unsaturated organic ligands can act as σ–donors or π–acids, increasing or decreasing electron density on the metal.[6] Alternatively, another view may also be taken: the metal centre perturbs the electronic profile of the ligand, and permits radical reactions of the ligand that may be inaccessible in the absence of metal–coordination. The reactions are thus influenced by the steric and electronic properties of both the metal and the ligand.

Obviously, this offers substantial flexibility for fine–tuning the reactivity of organometallic reagents. For complexes whose ligands permit variable bonding modes, changes in ligand binding or geometry can alter the electron count at the metal so that several different radical species can be in equilibrium, thus offering the possibility of several reaction types or sequences in a single reaction mixture.

Organometallic compounds are capable of acting in a bilateral fashion: in addition to serving as radical initiators, they are capable of acting as radical acceptors and, as such, the steric and/or electronic profile of the template can be exploited to mediate novel radical reaction sequences.

A. *Ligand–centred free–radical addition reactions of transition metal complexes*

Organometallic complexes are indispensable tools to organic chemists: the most prevalent method for generating carbon–centred radicals is through the intermediacy of organometallic complexes, especially by homolysis of a C–X, C–S, or C–OR bond via a stannane. Transition metal promoted radical reactions are usually terminated with the introduction of functionality into the final product,[1c] whereas in most organic radical reactions, the radical centre in the product is reduced by hydrogen atom transfer, resulting in overall loss of functionality in the transformation.

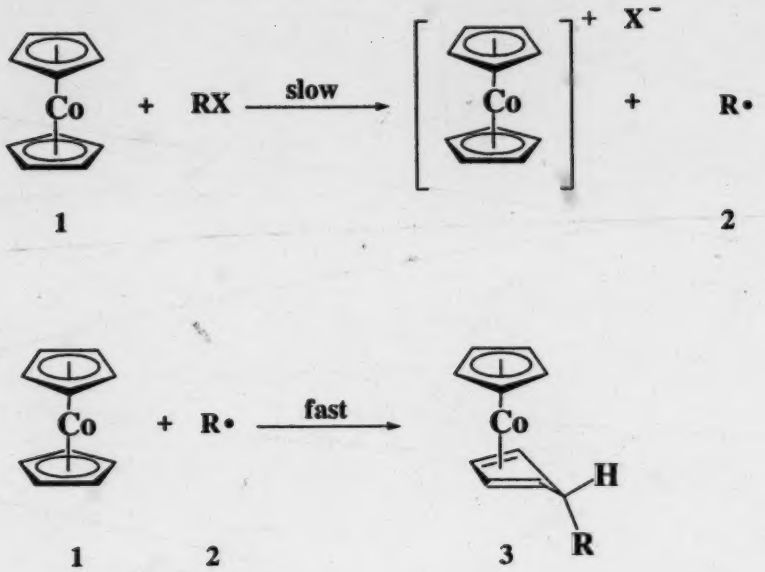
Organometallic radicals can participate in a myriad of processes, including atom transfer, radical coupling, associative substitution, electron transfer, metal–alkyl homolysis and migratory insertion.[6] The more common metal–centred radical reactions involve dimerization by formation of metal–metal bonds, halogen atom abstraction, and

hydrogen abstraction. Because the early emphasis in radical organometallic chemistry was primarily concerned with metal–centred reactivity, the literature contains extensive examples of this type. However, although there are relatively few examples of radical reactivity of coordinated ligands, this sort of chemistry is becoming more common, as a wider variety of reactions are being observed.[1b]

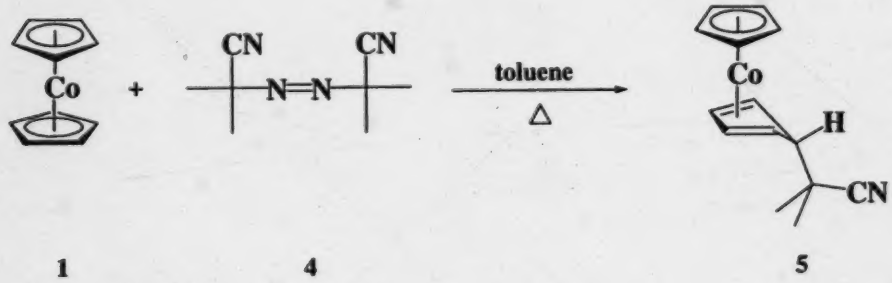
In 1969, Herberich and Schwarzer proposed[7] a two–step radical mechanism for the reaction of alkyl halides with cobaltocene **1**, in which the transition–metal compound serves to both reduce the alkyl halide and trap the subsequently formed alkyl radical **2** as a product of ligand alkylation **3** (Scheme **1.1**).[8] They also described the first deliberate addition of an organic radical to a metal–bound ligand.[9] Thermal decomposition of azobis(isobutyronitrile) (AIBN) **4** in the presence of cobaltocene **1** affords cyclopentadienyl–[5–*exo*–(1–cyano–1–methylethyl)cyclopentadiene]cobalt **5** almost quantitatively (eq. **1.1**). Free radical addition has more recently been demonstrated on other types of ligands, including α,β unsaturated Fischer carbene complexes,[10] arene ligands,[11] η^2–alkenyne ligands,[12] η^3–allyl ligands[13] and others.[1b]

There are many other modes of radical reactivity known for metal–complexed ligands. One mode of reactivity available to cobalt–complexed propargyl radicals is radical–radical coupling through the terminal carbons (Scheme **1.2**). In this case, each of the triple bonds of bis(propargyl) compound **6** were complexed to cobalt dimer **7**, leaving the termini bearing the hydroxyl groups free to undergo reaction. Treatment with strong acid followed by reduction with Zn or benzophenone ketyl affords a presumed transient

Scheme 1.1



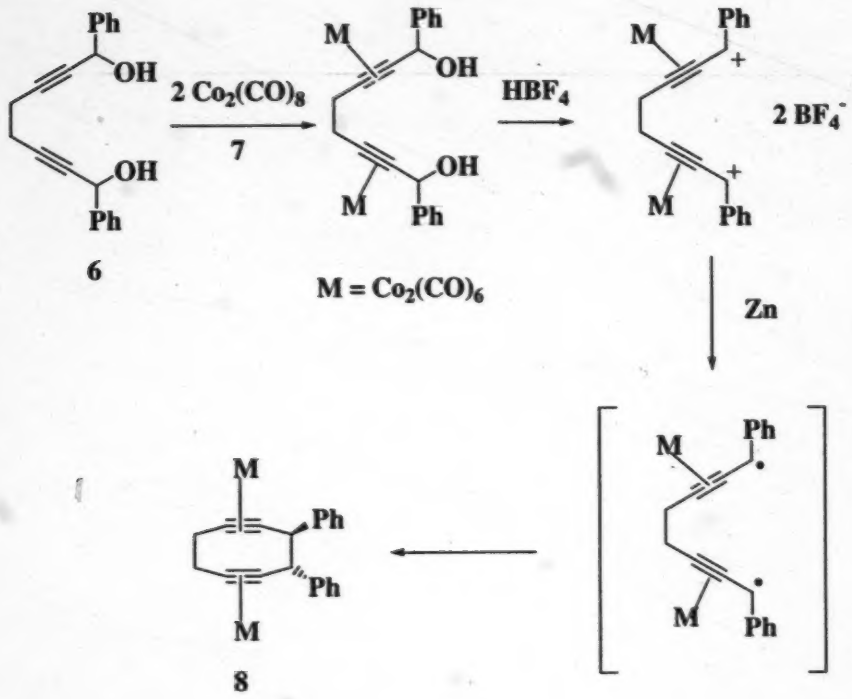
α,ω–propargyl di–radical that undergoes radical coupling to afford the 1,5-diyne structure **8** (Scheme **1.2**).[14] This procedure was developed to circumvent the poor regioselectivity associated with standard organic propargyl radical coupling.



eq. 1.1

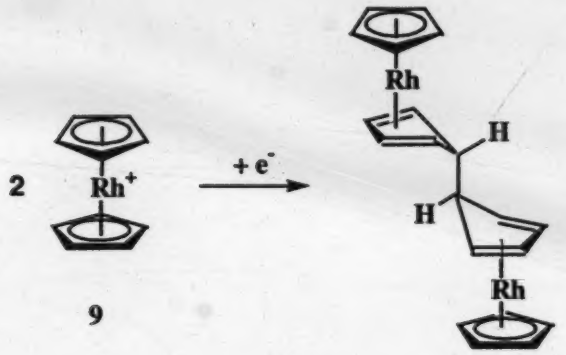
The two most common modes of reactivity available to odd–electron organometallic species are dimerization *via* ligand–ligand coupling or metal–metal

Scheme 1.2



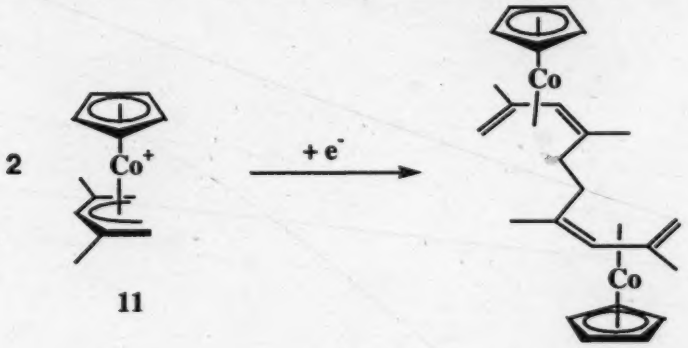
coupling. In the case of most 19e$^-$ complexes,[1a] dimerization occurs through the ligands. This dimerization is especially important in 19e$^-$ organometallic systems with polyhapto hydrocarbyl ligands. Ligand polyhapticity allows electron density to be spread out over many atoms, stabilizing the odd–electron complex. Dimerization through the ligands lowers the hapticity and decreases the electron count at the metal centre. An example is the coupling of cyclopentadienyl ligands to form the neutral 18e$^-$ complex **10** that occurs upon one-electron reduction of rhodocenium cation **9** (eq. **1.2**).[15] Open polyhapto ligands

also experience dimerization from 19e⁻ intermediates. For example, an end–to–end dimerization of the open η^5–pentadienyl ligand rather than the closed η^5–



9 10 eq. 1.2

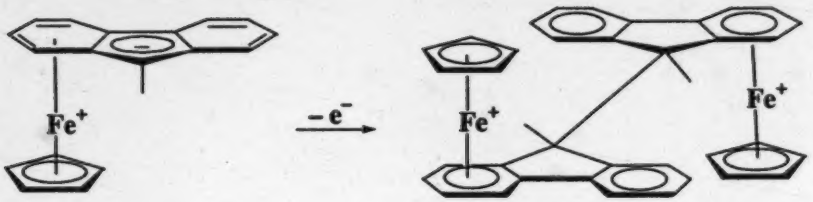
cyclopentadienyl ring occurs when cation **11** undergoes one electron reduction (eq. **1.3**).[16]



11 eq. 1.3

Likewise, ligand–ligand coupling is observed for cationic 17e⁻ complexes with polyhapto ligands. For example, neutral 18e⁻ iron fluorenyl complex **12** undergoes ligand–centred dimerization upon one electron oxidation (eq. **1.4**).[17]

In contrast, neutral 17e⁻ organometallic complexes tend to experience metal–based dimerization.[18] An exception to this trend is Ogoshi and Stryker's observed

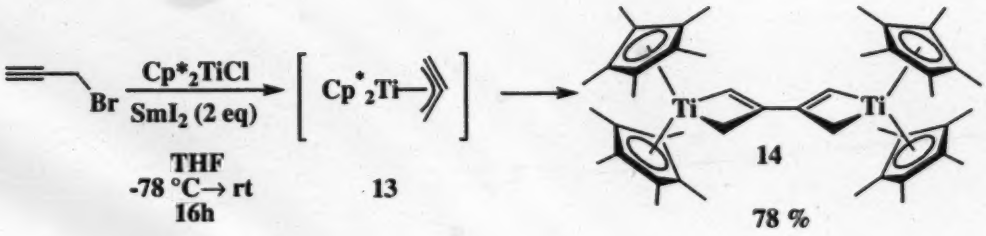


eq. 1.4

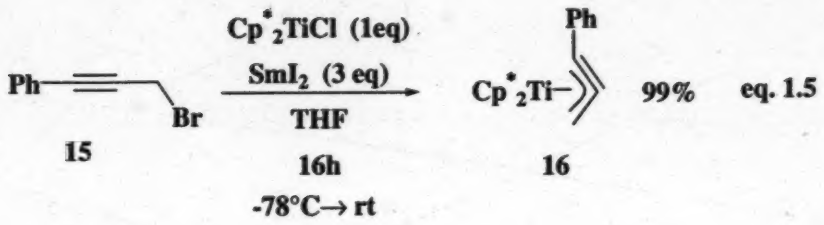
12

formation of dimeric titanium complex **14** (Scheme **1.3**).[19] Dimer **14** is proposed to arise from the coupling of the central carbons of transient $17e^-$ species **13**, formed in the reaction of propargyl bromide, bis(pentamethylcyclopentadienyl)titanium(III) chloride and samarium diiodide. Evidence for the titanium(III) propargyl intermediate and this

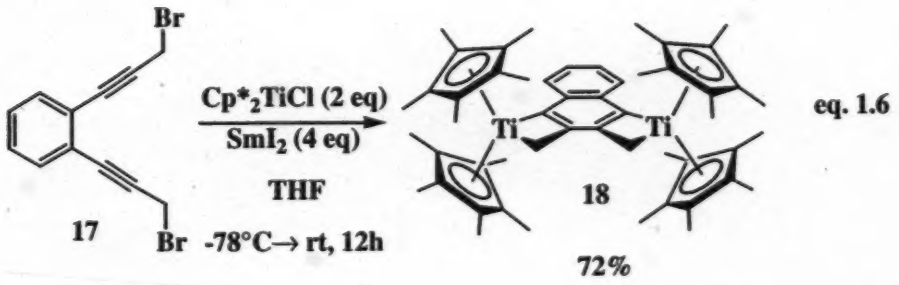
Scheme **1.3**



mode of reactivity is provided by the isolation of analogous stable titanium(III) compound **16**, which does not undergo dimerization, from the reaction of 3–bromo–phenylpropyne with bis(pentamethylcyclopentadienyl)titanium(III) chloride and samarium diiodide (eq. **1.5**),[19] and from titanacyclobutene formation by free–radical alkylation of the reactive complex **13** and related intermediates. Although the phenyl–substituted propargyl compound **16** prefers to remain an odd–electron titanium(III) compound and does not dimerize, an interesting pseudodimeric product is formed when



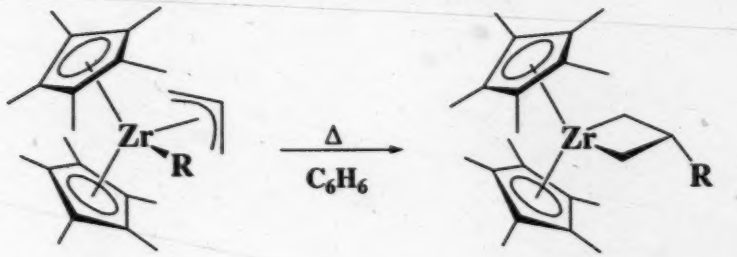
related 1,2–bis–(3–bromopropynyl)benzene **17** is subjected to the same reaction conditions. Tetracyclic naphthalene derivative **18** is formed by intramolecular coupling (eq. **1.6**).[19] Both substrates **15** and **17** are aryl–substituted propargyl bromides, and the difference in reactivity is noteworthy. The reason why one remains a monomeric odd–electron compound while the other "dimerizes" to form a titanium(IV) product is unclear. The reason for pseudo–dimer formation in the latter is more likely to be the result of a favourable entropic regime than the gain of resonance energy from aromatization: in this thesis we report that pseudo–dimer formation is also observed using substrates that do not lead to an aromatic product (page 120).



Permethyl zirconocene bis(allyl) complexes undergo ligand rearrangement under thermal and photolytic conditions to afford β–substituted zirconacyclobutane complexes.

This conversion is thought to involve a transient organic radical species that attacks zirconium–bound η^3–allyl at the central carbon. When [Cp^*_2Zr(allyl)R] (R = allyl, benzyl, crotyl) **19** is gently heated in benzene, the starting material is consumed and a β–substituted zirconacyclobutane **20** is produced in high yield (eq. **1.7**).[20] The zirconacyclobutane product is the apparent result of the migration of R• to the central carbon of the η^3–allyl moiety by either an intramolecular radical pair mechanism, or by an intermolecular process. Complexes in which the R group is either methyl or phenyl do not undergo rearrangement. The less electron–rich substrate [$Cp_2Zr(allyl)_2$] does not react in this fashion, either.

In an effort to oxidize η^3–allyl titanocene complex **21** with lead(II) chloride to form the expected titanium(IV) species, $Cp^*_2Ti(C_3H_5)(Cl)$ **22**, Casty and Stryker



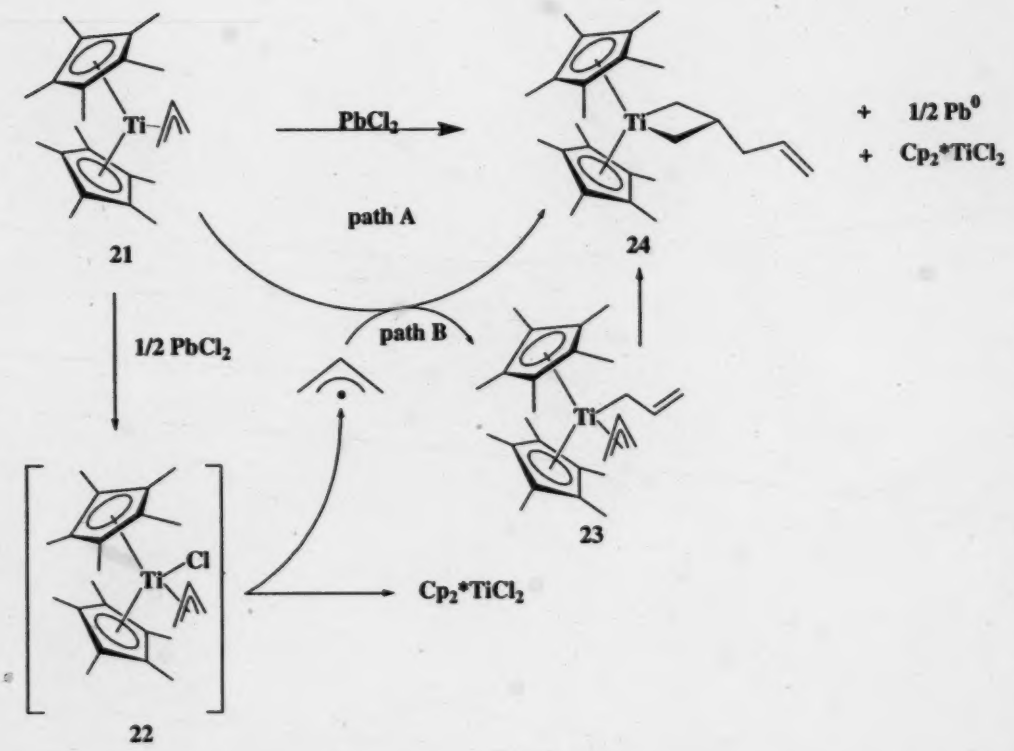
eq. 1.7

19 **20**

observed the formation of β–allyl titanacyclobutane complex **24** along with the corresponding dichloride complex in a 1:1 ratio (Scheme **1.4**).[13] This important but unexpected transformation was rationalized by the following proposed mechanistic pathway. The transformation involves oxidation of the titanium(III) allyl complex as a first step, giving putative chloro allyl intermediate **22** by reaction with lead(II) chloride.

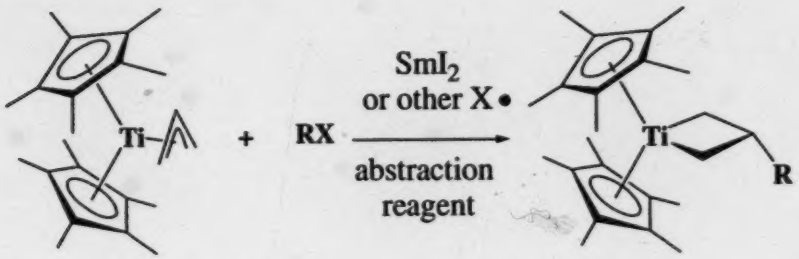
The transient titanium(IV) species **22** ejects allyl radical which may then either alkylate the central carbon of the η^3–allyl ligand bound to a second molecule of **21** (path A), or attack the metal centre of **21** to form unstable **23** (path B). Bis(allyl) complex **23** may in turn either eject allyl radical into the bulk solvent or undergo internal rearrangement, presumably *via* a radical pair, to form titanacyclobutane complex **24**. Encouraged by the

Scheme **1.4**



unique and highly regioselective reactivity of this radical alkylation, Casty and Stryker investigated a series of reactions whereby an organic radical was generated from a halide precursor in the presence of $Cp^*_2Ti(\eta^3\text{–}C_3H_5)$ **21**.[13] In all cases, the radical addition

product is exclusively the result of attack at the central carbon of the allyl ligand (eq. **1.8**) to form titanacyclobutane complexes **25**. Attack at the metal is not observed as the titanium (allyl)alkyl product would decompose by ejecting the stabilized allyl radical, leading to products derived from the titanium alkyl species. In an effort to extend the



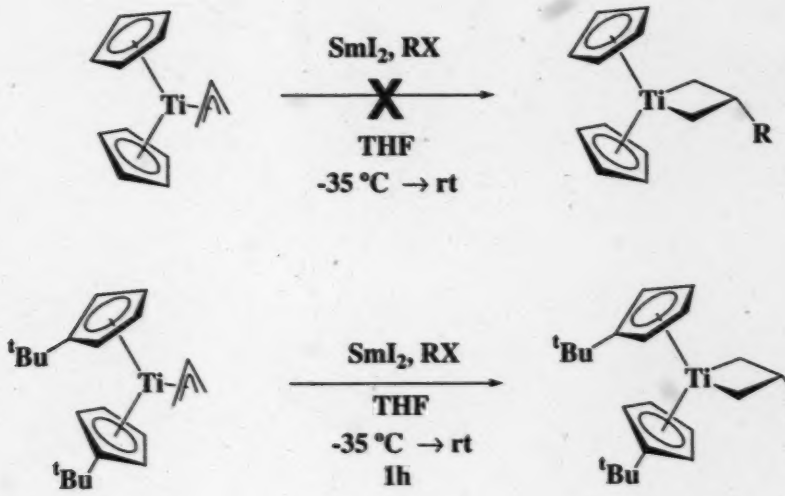
21 **25** **eq. 1.8**

RX = $PhCH_2Cl$, Ph_2CHCl, PhCH(Me)Cl, ^{i}PrI, ^{n}PrI, ^{t}BuI, CyI

scope of the reaction, the more readily accessible $Cp_2Ti(\eta^3\text{–}C_3H_5)$ complex was studied as a possible reaction template. As with the zirconocene rearrangements noted above, the less electron–rich $Cp_2Ti(\eta^3\text{–}C_3H_5)$ fails to undergo titanacyclobutene formation under the reaction conditions optimized for **21**[21] (Scheme **1.5**). However, $(^{t}BuCp)_2Ti(\eta^3\text{–}C_3H_5)$ reacts under the optimized radical alkylation conditions to afford good yields of central carbon addition product. Since the electron richness of a cyclopentadienyl ring increases with the number of alkyl substituents,[22] it is reasonable to propose that there is a minimum electron density requirement at the metal centre for successful central carbon alkylation.[23] The substitution of two pentamethylcyclopentadienyl ligands for two

cyclopentadienyl ligands on titanocene is approximately equivalent to a one–electron reduction of the complex.[22] The extra electron density in the former case might act to destabilize the singly occupied molecular orbital of the metal compound, increasing the ligand character of the orbital (SOMO), making it more prone to radical attack.

Scheme 1.5



In the $Cp_2Ti(\eta^3\text{–}C_3H_5)$ complex, the lack of electron richness may attenuate the one–electron d→π* back–bond to the extent that $\eta^1 \leftrightarrow \eta^3$ isomerism (Figure **1.1**) occurs rapidly or favours the η^1–form, decreasing the concentration of the reactive η^3–allyl species prohibitively. The η^1–allyl complex may then suffer alkylation at the metal or undergo selective halide abstraction followed by release of alkyl radical into the medium. Formation of the titanium(IV) products in the more electron rich

pentamethylcyclopentadienyl series also provides a greater thermodynamic driving force than that provided by the less electron rich cyclopentadienyl complexes.

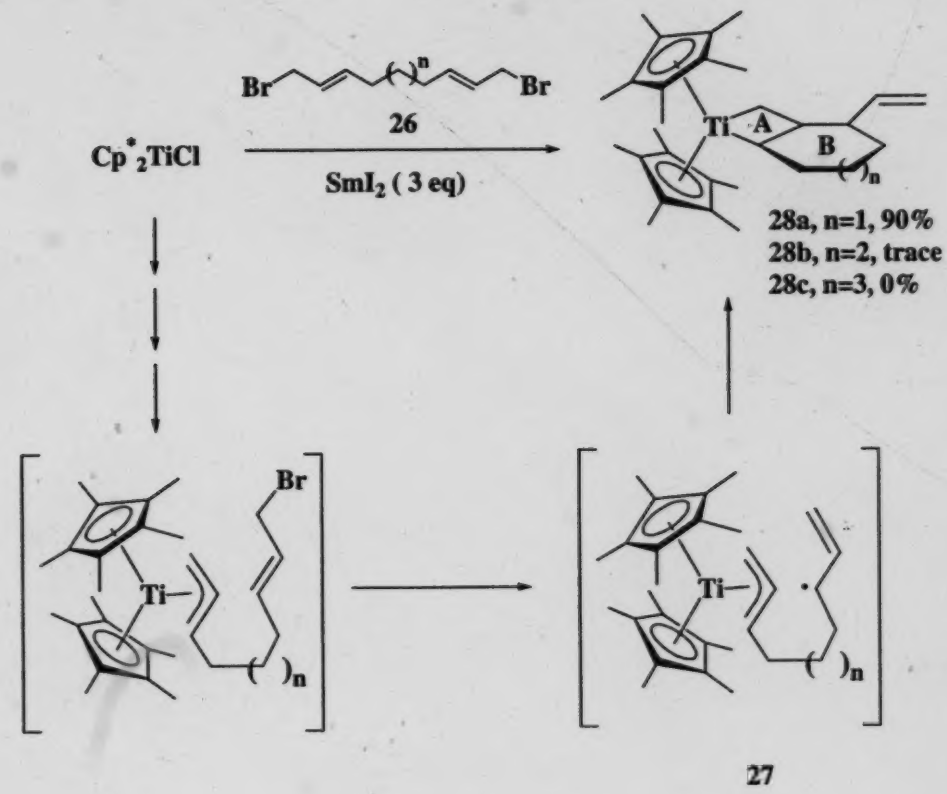
Figure **1.1**

η^3-η^1 Isomerization of allyl ligands

η^3-coordination mode η^1-coordination mode

Free–radical addition to a bound allyl ligand can also occur intramolecularly to furnish bicyclic titanacyclobutanes **28** in high yield[24] (Scheme **1.6**), but the reaction is not general. The η^3–allyl moiety is generated *in situ* from one end of the α,ω–bis(allylbromide) substrate **26**. The reduction of the other end of the chain results in an allylic radical, **27**, which then attacks the central carbon of the bound allylic moiety to form **28**. The scope of this cyclization reaction is limited: the reaction proceeds only in the case for which the B–ring contains six carbons. This reaction is the only successful example of a substituted allyl ligand submitting to radical alkylation in the bis(pentamethylcyclopentadienyl) titanocene series.

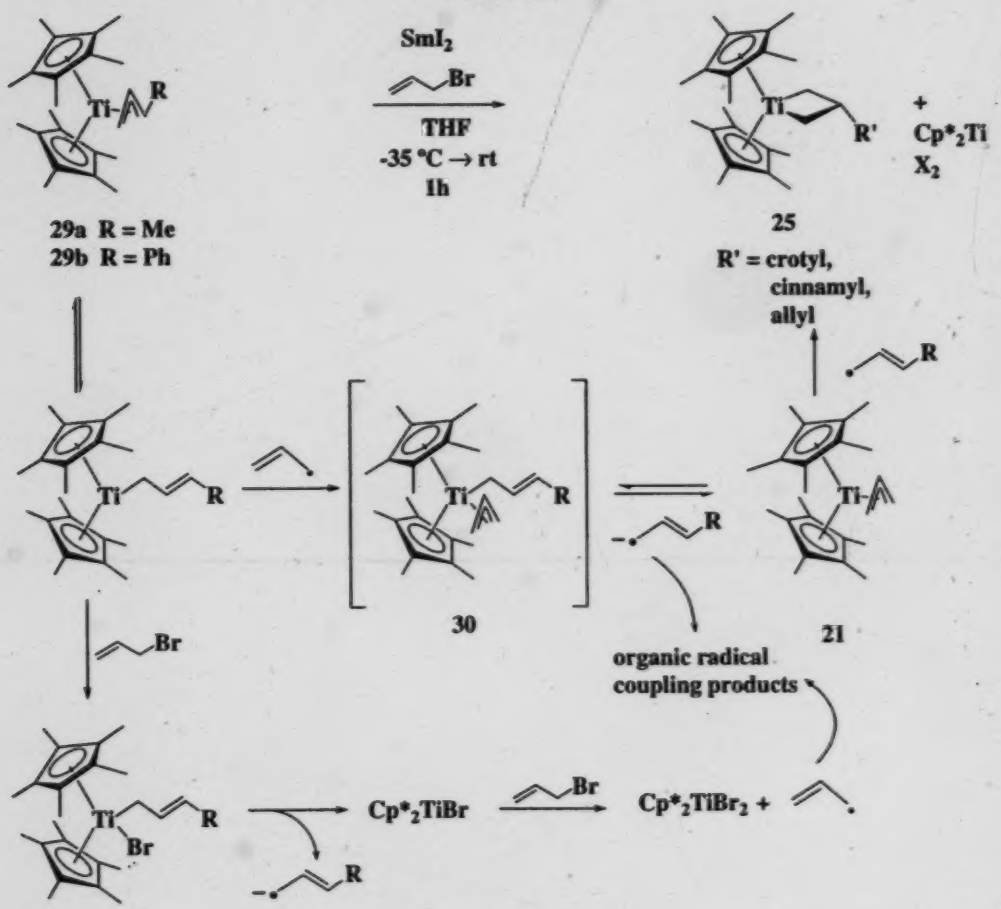
Scheme 1.6



Attempts to alkylate the 1–methylallyl (crotyl) and 1–phenylallyl (cinnamyl) complexes **29a** and **29b** (Scheme **1.7**) by treatment with allyl bromide and the radical initiator SmI_2 failed to produce the desired α,β–disubstituted titanacyclobutane products, instead producing only β–allyl substituted titanacyclobutane **25** complex in low yield.[25] Metal–centred reactivity is thought to frustrate the desired reaction, producing unstable

bis(allyl) complex **30** rather than providing direct ligand alkylation. The overall process is thought to proceed by the following sequence of events: despite the bulk of the

Scheme **1.7**



pentamethylcyclopentadienyl ligand set, the allyl radical, formed by halide abstraction from allyl bromide, attacks the metal centre of the titanocene complex rather than the ligand presumably due to the open coordination site provided by the $\eta^1 \leftrightarrow \eta^3$ equilibrium. This results in the formation of the unstable species **30**, which is in

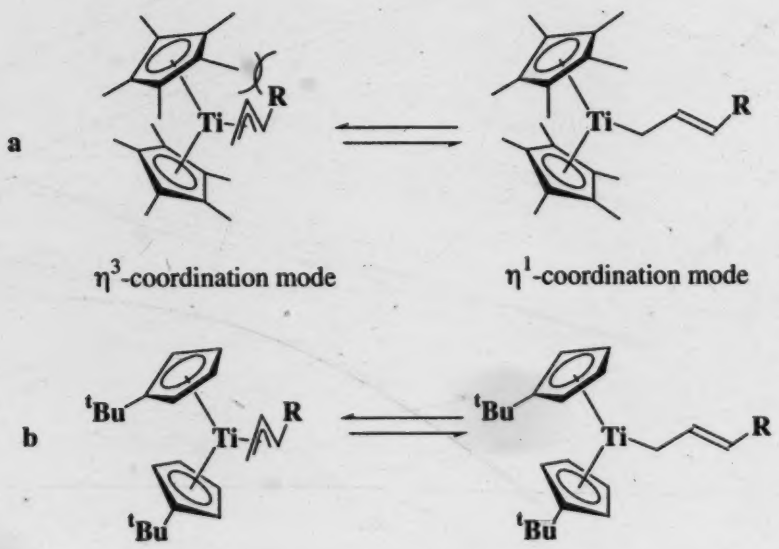
equilibrium with starting complex **29** and unsubstituted allyl complex **21**. Complex **30** preferentially ejects the more substituted allyl ligand (crotyl or cinnamyl) to form η^3–allyl complex **21**. Free crotyl or cinnamyl radicals competitively dimerize to form organic coupling products, as well as attack titanium(III) complex **21** to form the mono–substituted product, **25**. Halide abstraction by the titanium(III) complexes **31** and **32** lead to ejection of allylic radicals and the formation of $Cp^*_2TiX_2$.

The observation that substituted allyl ligands are not tolerated and do not undergo central carbon alkylation in the bis(pentamethylcyclopentadienyl)titanium(III) series represents an important limitation of this methodology. One hypothesis to explain this behaviour invokes both steric and electronic arguments.[26] Substituents on the allyl moiety may not be compatible with the steric requirements of the bulky pentamethylcyclopentadienyl ancillary ligand set, causing the equilibrium between η^3– and η^1–coordination modes[26] to be shifted towards the undesired η^1–mode (Figure **1.2**a). The less bulky *tert*–butylcyclopentadienyl and cyclopentadienyl ligands, while not providing as much steric opposition to the allylic fragments, are unable to provide the minimum electronic profile required to anchor the substituted allyl ligand in the η^3–coordination mode (Figure **1.2**b).[13,19]

Central carbon radical alkylation of substituted allyl complexes does occur in other ligand series. Electron–rich ligands seem to facilitate substituted allyl alkylation reactions. The purportedly more electron–rich bis(2–piperidinoindenyl)titanium(III) complexes **31** allow organic radical attack on the ligand to form 2,3–disubstituted titanacyclobutane complexes (eq. **1.9**, and Table **1.1**).[26,27] Ansa–titanocene complexes

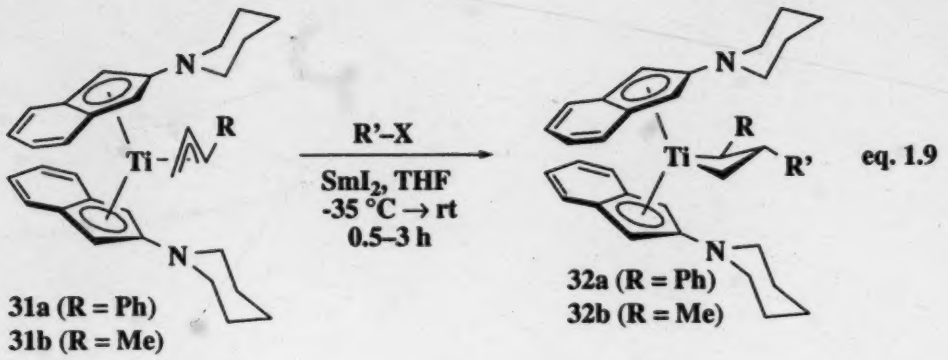
meso–ansa[1]–bis(3,3'–trimethylsilylcyclopentadienyl)titanium **33** also undergo alkylation of substituted allyl ligands by organic free radicals (eq. **1.10**).[25]

Figure **1.2**



B. ***Central Carbon Alkylation of Titanium η³–Propargyl/Allenyl Ligands.***

It is interesting to note that while 1–methyl– and 1–phenyl–η^3–allyl ligands generally fail to undergo central carbon radical alkylation in the pentamethylcyclopentadienyl, *tert*-butylcyclopentadienyl , and cyclopentadienyl series, the analogous η^3–propargyl ligands in all three titanocene complexes succumb to organic radical alkylation, affording the 2,3–disubstituted titanacyclobutene products, generally in high yields[19,28,29] (eq. **1.11**). A



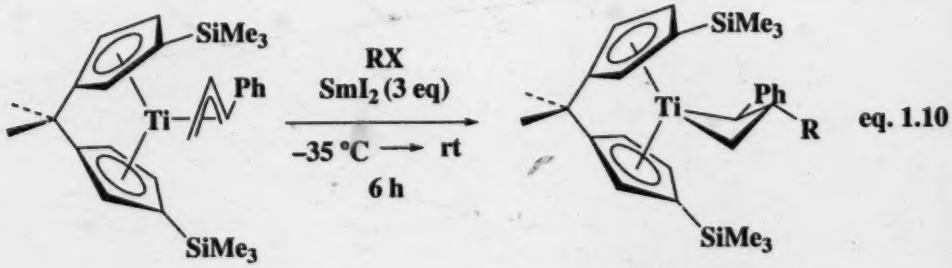
31a (R = Ph)
31b (R = Me)

32a (R = Ph)
32b (R = Me)

eq. 1.9

Table 1.1 Radical alkylation of indenyl π-allyl complexes **31**

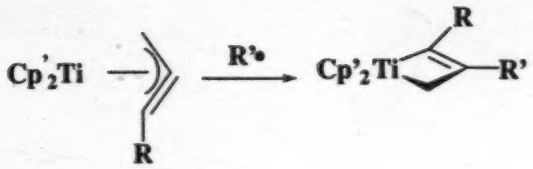
starting material	R'X	% yield
19a	^{i}PrI	72
19a	CyI	80
19a	^{t}BuCl	88
19b	^{i}PrI	69
19b	CyI	70
19b	^{t}BuCl	36



33

R = ^{i}Pr (73%)
R = Cy (95%)

eq. 1.10

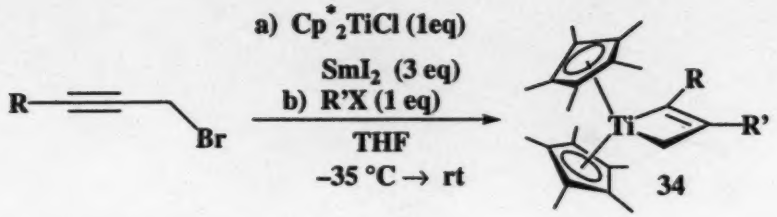


eq. 1.11

Cp' = Cp*, ^{t}BuCp, Cp

collection of products from similar reactions in all three templates is tabulated for comparison in Chapter 2, Table 2.1.

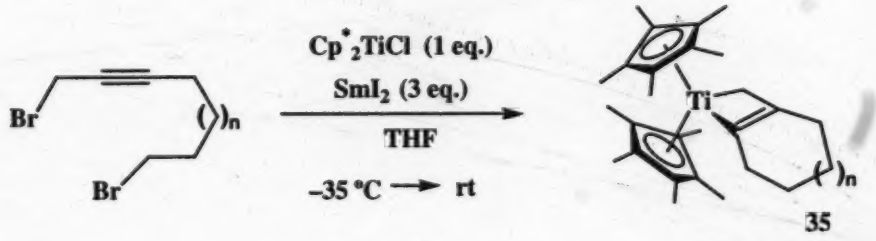
Ogoshi and Stryker found that treatment of a solution of bis(pentamethylcyclopentadienyl)titanium(III) chloride and samarium diiodide at –78 °C with 3–bromo–1–phenyl–propyne followed by addition of benzyl chloride affords the 2,3–disubstituted titanacyclobutene **34** in high yield (eq. **1.12**, and Table **1.2**).[19] When butynyl bromide is used in place of 1–phenyl–3–bromopropyne, the yield is essentially quantitative. The reactive η^3–propargyl ligand is generated *in situ* under the reaction conditions from the propargyl halide precursors and the titanocene(III) chloride.[30] A range of organometallic products has been synthesized using this propargyl chemistry. Intramolecular alkylation of propargyl ligands is also successful in titanium–mediated organic radical alkylation reactions. The reactions proceed in generally high yields to form bicyclic titanacyclobutenes **35** (eq. **1.13**). Ring sizes of five,[28] six,[19] and, surprisingly, seven through ten[28] have been reported in the pentamethylcyclopentadienyl series.



(eq. 1.12)

Table 1.2 Radical alkylation of Cp* titanocene propargyl π–complex

R	R'	yield (%)
CH_3	BnCl	99
CH_3	^{i}PrI	99
CH_3	$CH_3C{\equiv}CCH_2Br$	99
Ph	BnCl	87
Ph	^{i}PrI	99
Ph	$PhC{\equiv}CCH_2Br$	93



eq. 1.13

n = 0 95%
n = 1 100%
n = 2 98%
n = 3 96%
n = 4 92%
n = 5 85%

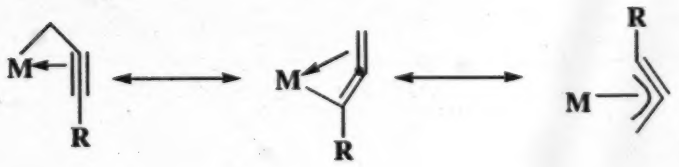
Detailed considerations: structure and bonding of η^3–propargyl/allenyl ligands. Since propargyl radical **36** and allenyl radical **37** are simply different canonicals of the same species, the corresponding metal–bound π–complexes should properly be referred to as propargyl/allenyl complexes. The bonding may be represented as η^3–propargyl, η^3–allenyl, or a combination of both (Scheme **1.8**).

Scheme 1.8

a. propargyl/allenyl radical canonicals

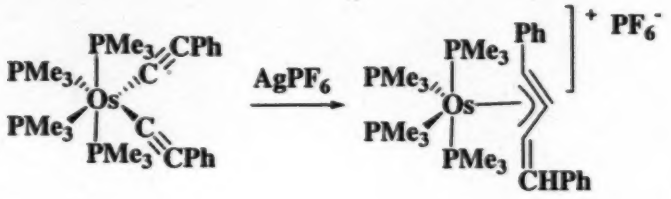
36 **37**

b. representation of η^3-propargyl metal complex



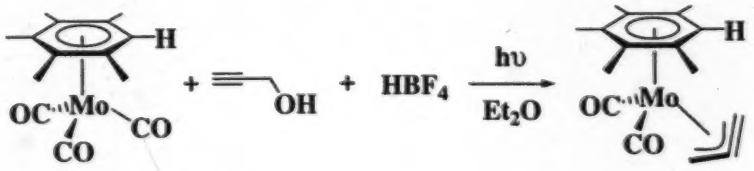
The first isolation of a transition metal compound with an η^3–bound propargyl moiety was the butenynyl complex described by Werner.[31] An oxidative coupling reaction of two alkynyl ligands in the osmium complex cis–$(PMe_3)_4Os(CCPh)_2$ **38** results from treatment with equimolar $AgPF_6$, to afford $[(PMe_3)_4Os(\eta^3\text{–}PhCCC{=}CHPh)]PF_6$ **39** (eq. **1.14**). The first transition metal complex produced with a simple η^3–propargyl/allenyl ligand was described by Krivykh.[32] After subjecting a mixture of $(\eta^6\text{–}C_6Me_5H)Mo(CO)_3$ **40**, propargyl alcohol, and $HBF_4{\bullet}OEt_2$ to UV irradiation,

complex **41** was isolated (eq. **1.15**).[32a] Using this same method, the synthesis of similar tungsten and rhenium compounds was also realized.[32b]



38 **39** eq. 1.14

When coordinated in a trihapto fashion, propargyl/allenyl ligands are bent rather than linear. The η^3–bonding modes of various propargyl/allenyl ligands have been described.[33] The main structural difference between η^3– allyl and propargyl/allenyl

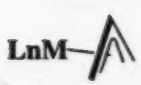


40 **41** eq. 1.15

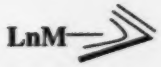
complexes is that the propargyl/allenyl ligand is essentially coplanar with the metal, while allyl ligand is bound "side–on" *via* the π–system (Fig. **1.3**). Spectroscopic evidence shows that, for different metals, different canonical structures are more dominant. A comparison of three mononuclear metal η^3–propargyl/allenyl complexes, $Cp_2Zr(Me)(\eta^3\text{–}PhCCCH_2)$[34] (**41**), $(\eta^6\text{–}C_6Me_5H)Mo(CO)_2(\eta^3\text{–}C_3H_3)$[32] (**40**), and $[(PPh_3)_2Pt(\eta^3\text{–}PhCCCH_2)]O_3SCF_3$[35] (**42**) illustrates these differences (Table **1.3**).[33]

The three carbons of the propargyl/allenyl ligand form a C–C–C bond angle in the range of 150–155° . This is considerably greater than that found for the η^3–allyl complexes[26]

Figure 1.3



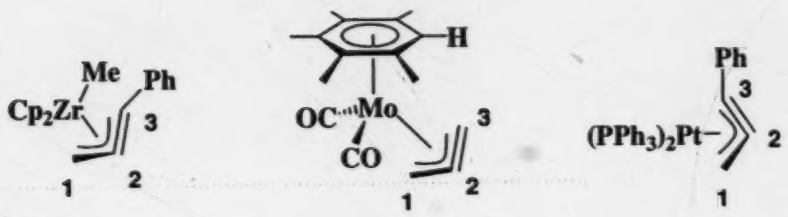
Bonding in η^3-allyl complex



Bonding in η^3-propargyl/allenyl complex

and reflects the presence of a central carbon which has substantial sp–character. The distance from C1 to central carbon atom C2 is shorter than the single bond of a propargyl species (1.47 Å) but longer than the double bond of an allenyl species (1.31 Å).[36] In the Group 4 zirconium species, this bond is the shortest of the three examples, suggesting that the allenyl canonical makes an important contribution. The C2–C3 bond distance (1.259 Å) is greater than the triple bond length found in propyne (1.21 Å) but less than that expected for a purely allenyl species.[36] These data suggest that the true bonding picture must take into account both canonical representations. The metal–carbon distances are also significant. The metal–carbon distances for all three species show that the hapticity is fairly represented as η^3: the three metal–carbon bond distances within each complex are very similar. The Group 4 zirconium species shows the largest deviation in the metal to carbon distances: the distance to C1 is slightly longer than to the other two carbon atoms.

Table 1.3 Comparison of Selected Parameters of Three Organometallic Propargyl Complexes

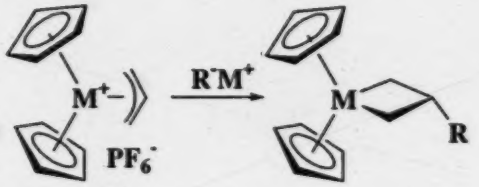


42 **41** **43**

Complex #	C1–C2	C2–C3	M–C1	M–C2	M–C3	C1–C2–C3 bond angle (deg)
42	1.344	1.259	2.658	2.438	2.361	155.4
41	1.380	1.236	2.340	2.282	2.319	150.9
43	1.39	1.23	2.186	2.150	2.273	152

Central carbon alkylation of η^3–propargyl/allenyl ligands. The origin of propargyl/allenyl alkylative titanacyclobutene chemistry extends back to the first reported instance of central carbon addition to an η^3–allyl ligand 25 years ago. The first examples of central carbon alkylation involved the addition of hydride, methyl anion, and allyl Grignard to cationic tungsten and molybdenum complexes.[37,38] The π–allyl complexes **44** unexpectedly undergo alkylation exclusively at the central allyl position. No alkylation at the metal centre was observed due to the 18-electron metal centre (eq. **1.16** and Table **1.4**).

Organometallic η^3–allyl complexes have a rich and well–documented reaction chemistry. Allyl complexes, especially of palladium, facilitate a plethora of useful synthetic transformations.[39] The related mononuclear η^3–propargyl species are also of interest. Both η^3–allyl and η^3–propargyl transition–metal complexes have a variety of reactivity paradigms that define them. That nucleophiles can attack both the terminal



eq. 1.16

44

M = Mo, W

Table 1.4 Central carbon alkylation of π–allyl Mo and W complexes

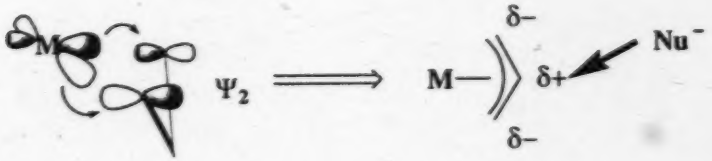
M	R	% yield
Mo	H	70
Mo	C_3H_5	60
W	H	80
W	C_3H_5	70

carbon of η^3–allyl complexes to provide elaborated alkenes,[39,40] and the central carbon to produce metallacyclobutanes and other products is now well established in the literature.[37,38,41] The reactivity patterns open to η^3–propargyl transition–metal complexes are similar: alkylation can occur at a terminal carbon[42] or at the central

carbon to give metallacyclobutenes,[19,43] coordinated alkynes, allenes, formally reduced η^3–allyl complexes,[35,43,44] and even zwitterionic complexes.[35]

A set of selectivity rules, the Davies–Green–Mingos (DGM) rules, were forwarded to explain the regioselectivity of nucleophilic addition based on a charge–control argument.[45] This argument posits that in electron rich systems, such as the d^2–compounds observed to undergo central carbon reactivity, a reasonable amount of $d\rightarrow\pi^*$ backbonding is expected, rendering the terminal carbons of the allyl ligand negative with respect to the central carbon (Scheme **1.9**). The relatively electrophilic central carbon would therefore be the site of nucleophilic attack. This theory has been reasonably successful in predicting reactivity in a majority of examples, however it fails to explain why compounds with no d–electrons, for example the titanocene(IV) allyl cations, have more recently been found to undergo central carbon alkylation.[13]

Scheme **1.9**

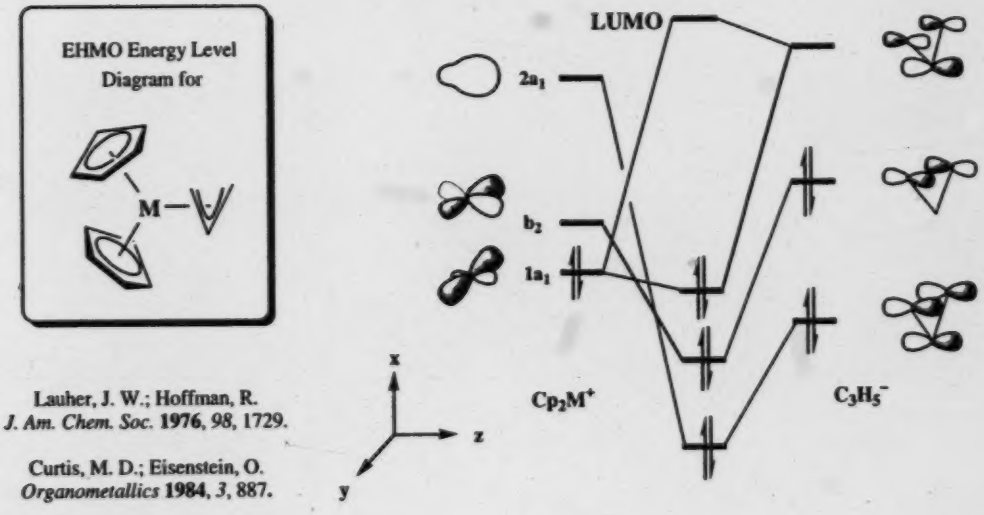


Several FMO analyses[46,47,48] have been undertaken *inter alia* to explain the general electronic structure of bent metallocene fragments and consequent effects on ligand bonding, to determine the factors that control the regioselectivity of nucleophile addition to a variety of η^3–allyl complexes, and to predict which other systems might

undergo central carbon or other reactivity patterns. These analyses use the symmetry characteristics of the MO fragments and calculated potential energies to predict and explain alkylation phenomena. In their analysis of a variety of π–allyl systems, Curtis and Eisenstein tentatively predicted that cationic, pseudo–tetrahedral, d^0 Group IV π–allyl complexes might undergo nucleophilic addition at the central carbon position.[47] This is an elaboration of Hoffmann's earlier EHMO theoretical treatment.[48] The approximate orbital overlap of an allyl fragment with a bent metallocene fragment is depicted in Figure **1.4**.

Figure **1.4**

a. d^2 bent-metallocene orbital diagram



Lauher, J. W.; Hoffman, R.
J. Am. Chem. Soc. **1976**, *98*, 1729.

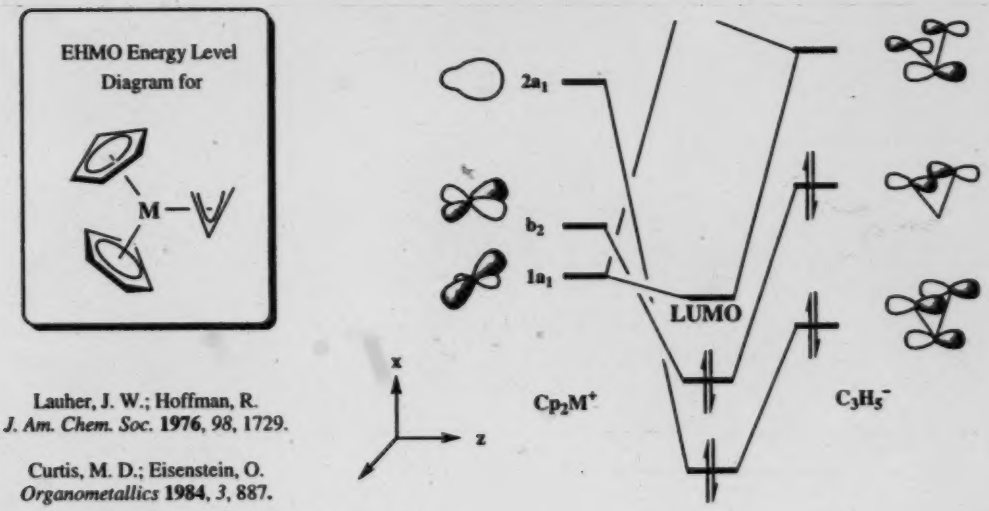
Curtis, M. D.; Eisenstein, O.
Organometallics **1984**, *3*, 887.

Green, J.C.
Chem. Soc. Reviews **1998**, *27*, 293.

For a d^2–metallocene fragment, such as the Mo compounds investigated by Green, the LUMO is formed from the anti–bonding combination of the metallocene $1a_1$ and the antibonding orbital of the allyl ligand (Figure **1.4a**).[46] The incoming nucleophile is directed to the centre carbon of the allyl ligand, which possesses the larger orbital coefficient than the termini. The electronic direction behind the two modes of reaction in the Group IV d^0-series can be surmised by inspection of the MO energy level diagram (Figure **1.4b**). The LUMO in this case is the bonding combination of the $1a_1$ orbital of

Figure **1.4**

b. d^0 bent-metallocene orbital diagram



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Curtis, M. D.; Eisenstein, O.
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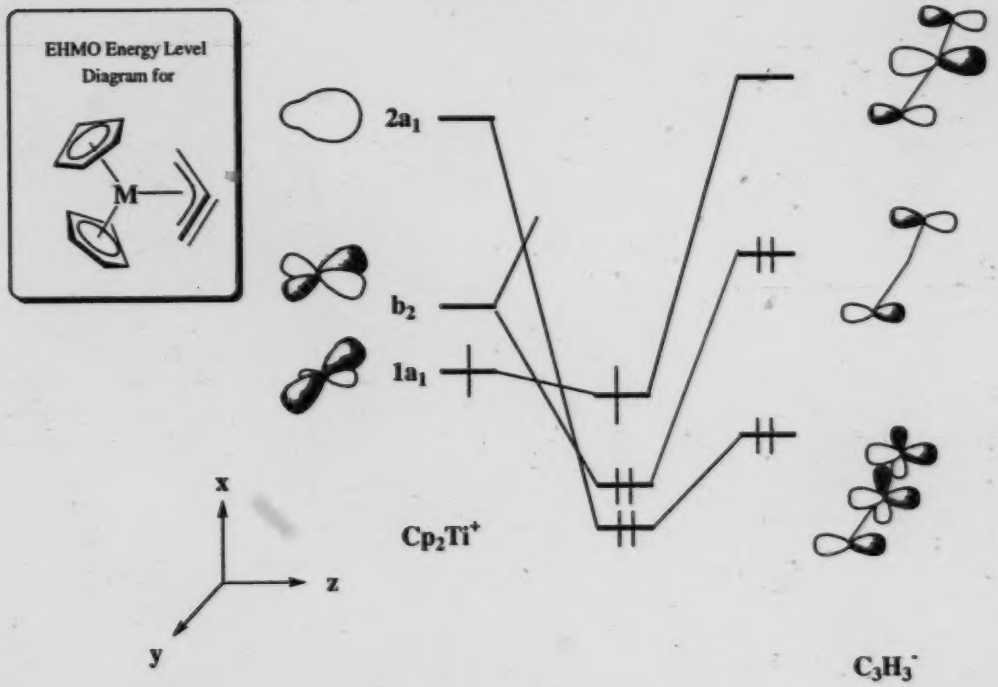
Green, J.C.
Chem. Soc. Reviews **1998**, *27*, 263.

the metal and the antibonding orbital of the allyl ligand. Because the LUMO is largely metal in character and the $1a_1$ orbital is directed outwards to the gap in the "wedge", the incoming nucleophile is directed there unless the metal is inaccessible. If access to the

metal centre is sterically impeded, the nucleophile is directed to the central carbon of the allyl ligand, which possesses the largest orbital coefficient in the LUMO. The radical alkylation mechanism is similar and follows from the same argument. In this odd–electron species, the SOMO (singly–occupied molecular orbital) is also the bonding combination of the metal $1a_1$ orbital and the antibonding orbital of the allyl (or propargyl/allenyl) ligand, and incoming radicals are directed to the central carbon of the ligand (Fig. **1.5**).

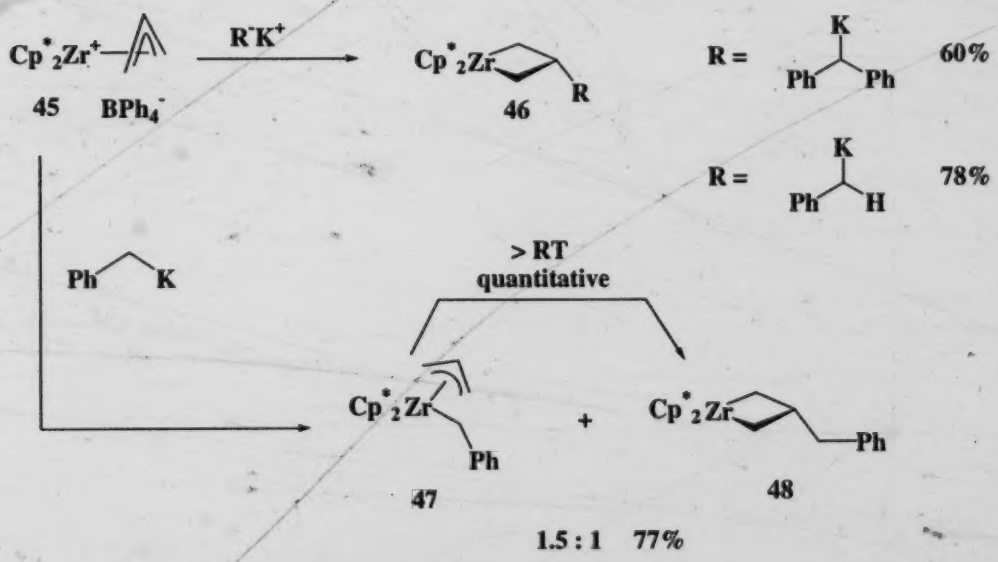
Figure **1.5**



The first example of this reactivity pattern in Group 4 compounds was noted by Stryker, *et al.*, corroborating Curtis and Eisenstein's prediction.[20] The reactions of cationic permethylated zirconocene and titanocene η^3–allyl complexes with a variety of

nucleophiles were studied. Nucleophilic addition proceeds in a manner dictated by the combined steric profile of the complex, the ancillary ligand set, and the incoming nucleophile. Thus, the use of methyl Grignard, MeLi, or allyl Grignard as the alkylating agent results in alkylation of the metal centre in zirconium complex **45**, despite the large pentamethylcyclopentadienyl ligands chosen, in part, to provide steric protection against this attack (Scheme **1.10**). Nucleophiles with a larger steric profile, specifically diphenylmethylpotassium and 1–phenylethylpotassium, regioselectively alkylate at the

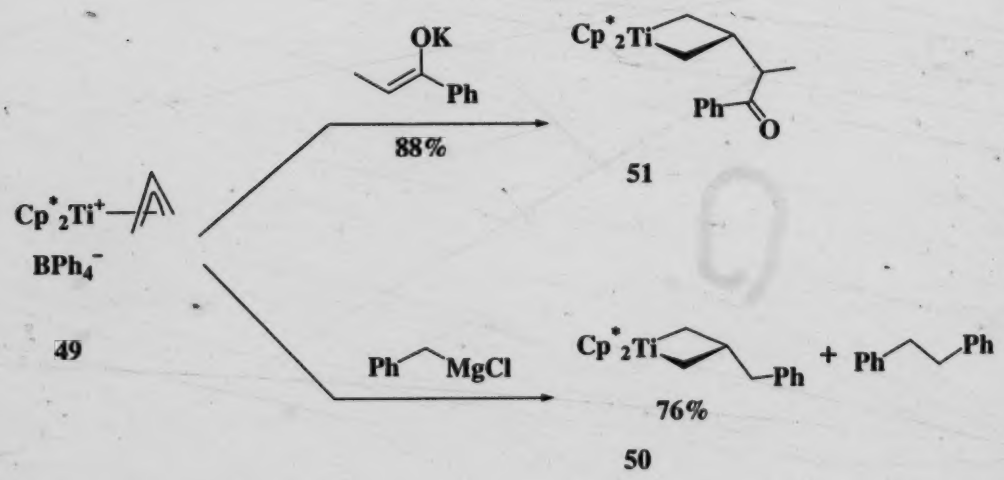
Scheme **1.10**



central carbon of the allyl ligand, giving metallacyclobutane complexes **46**. Benzyl potassium, a nucleophile with an intermediate steric profile, leads to a kinetic partitioning, with initial formation of a majority of the metal–alkylated product **47**. The metal–alkylated product transforms over time to the thermodynamically more stable

zirconacyclobutane complex **48**. In contrast, the cationic titanocene compound **49** undergoes alkylation exclusively at the allyl central carbon to afford the corresponding titanacyclobutane complexes (Scheme **1.11**).[13, 25] Reaction proceeds smoothly with both benzyl Grignard and the potassium enolate of propiophenone to afford compounds **50** and **51**, respectively. However, unlike the zirconium analogue, the reaction of allyl cation **49** with benzylpotassium leads to a mixture of titanacyclobutane complex **50** and diphenylethane. The latter presumably results from the oxidation of benzyl anion by the electrophilic titanium(IV) centre, followed by coupling of the resultant radicals.

Scheme **1.11**



The smaller ionic radius of the titanium centre coupled with the large pentamethylcyclopentadienyl ligand set effectively shields the metal centre from alkylation. Under radical alkylation conditions, the neutral d^1 species $Cp^*_2Ti(\eta^3\text{–}C_3H_5)$ and bis(2–piperindinoindenyl)$Ti(\eta^3\text{–}RC_3H_4)$ (R = Me, Ph) react at the central allyl

position to form titanacyclobutane complexes.[13,26,27b] There are now many other examples of metallacyclobutane formation by nucleophilic alkylation across the transition metal block.[37,38,49,50]

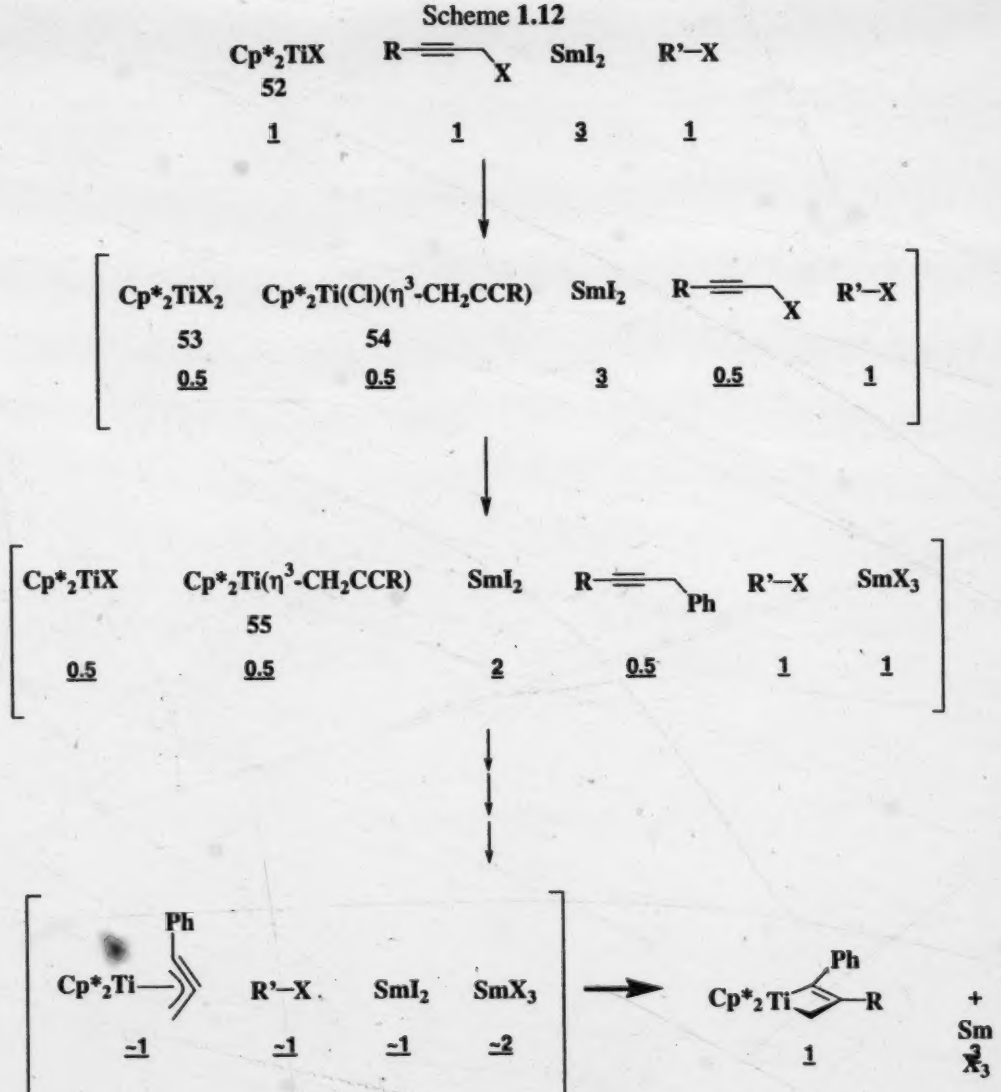
The η^3–propargyl/allenyl fragment is similar to the η^3–allyl with respect to the overlap of frontier molecular orbitals[48] (see Figure **1.5**, pg. 29). The overlap of the allyl basis set with the metal fragment orbitals should result in essentially the same electronic profile for the η^3–propargyl/allenyl ligand as for the η^3–allyl ligand, with the extra, orthogonal π–bond not contributing significantly to the overall reactivity. While no theoretical treatment of this particular thesis has been undertaken and this analysis is purely conjectural, the prediction has been upheld by experiment: η^3–propargyl/allenyl titanocene d^1 species indeed undergo radical alkylation at the central carbon.[19,28,29] That the reactivity may be altered slightly with respect to the allyl model is evidenced by the fact that in the propargyl series many reactions are available that are inaccessible in the allyl series. The fact that the η^3–propargyl/allenyl ligand submits to radical alkylation in cases where the allyl does not presumably results from slightly different bonding characteristics: allyl ligands, especially those with α–substituents, seem to be much more labile with respect to $\eta^1 \leftrightarrow \eta^3$ equilibrium. This may be a result of the orientation of the allyl ligand when bound in η^3–fashion to the metal: due to the side–on bonding, the α–substituent is directed towards the Cp' rings (see Figure **1.2**, pg. 16, and Figure **1.3**, pg. 23). A substituent on the α–position of the η^3–bound propargyl fragment, however, is in the "wedge" between the Cp' rings. Additionally, allyl ligands may not be bonded as strongly, and the η^1–structure is obviously unreceptive to central carbon alkylation.

There are favourable consequences, then, of the second double bond in the propargyl/allenyl case. Although orthogonal, it may perturb the physical environment, electronically anchoring the propargyl/allenyl ligand more securely to the metal, or somehow act to increase the radicophilic properties of the complex by better matching the orbital energies with that of the incoming radical.

Attack at the metal centre was observed in the cationic zirconocene allyl compounds if the nucleophile was of sufficiently diminutive steric profile.[20] This reactivity is ascribed to the mainly metal character of the LUMO.[48] In the cationic titanocene allyl series, only ligand alkylation was observed. This was attributed to the steric blockade provided by the large pentamethylcyclopentadienyl ligand set and the relatively smaller ionic radius of titanium compared to zirconium. In the corresponding propargyl chemistry, radical alkylation occurs only at the propargyl/allenyl ligand, and only at the central carbon. The absence of metal alkylation is noteworthy, especially considering the lack of steric protection afforded by the *tert*–butylcyclopentadienyl and cyclopentadienyl ligand sets. The direction of the incoming radical to the ligand suggests that the LUMO in these cases is perhaps more substantially ligand in character.

The samarium diiodide–mediated radical alkylation of propargyl/allenyl ligands of titanocene complexes, discussed in the previous section, is rationalized by the following speculative mechanistic pathway (Scheme **1.12**).[19] The reaction can be divided into two main domains: (i) generation of the η^3–propargyl/allenyl titanium(III) intermediate **55**, and (ii) organic radical formation and addition. The initial reduction of

Scheme 1.12



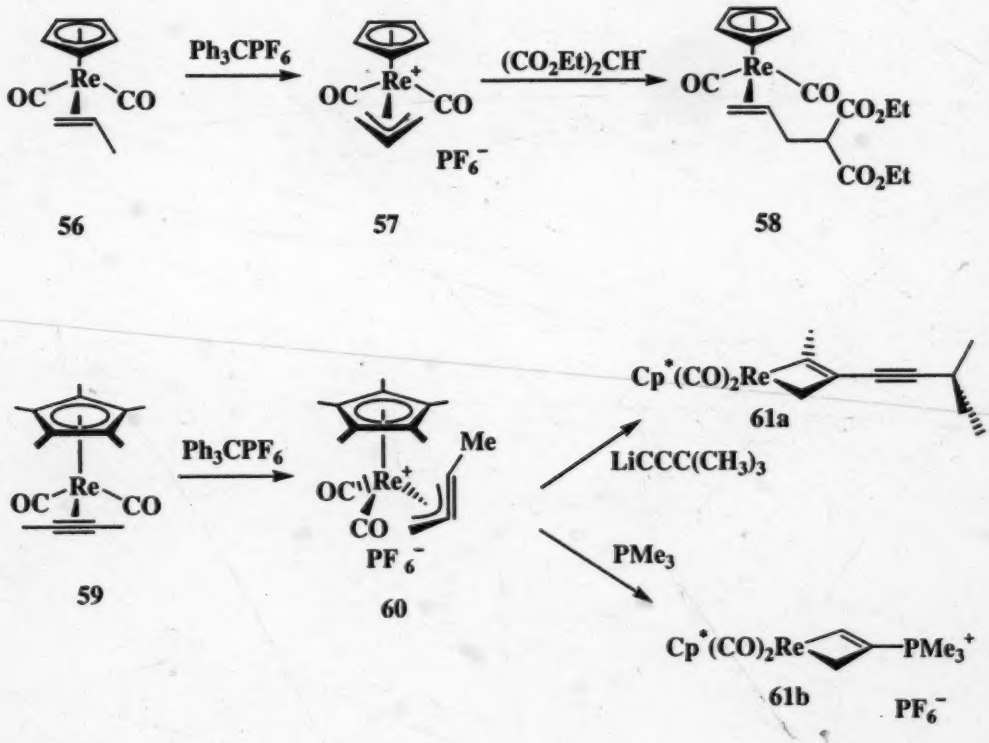
‡: numbers in Times font are compound designators, underlined numbers are approximate relative ratios

the propargyl halide is thought to be induced by the titanocene species **52**, rather than by direct reaction with SmI_2. Control experiments show that at the low reaction temperature, propargyl halide fails to undergo reaction with SmI_2, even over prolonged periods. Addition of propargyl halide to a solution of bis(pentamethylcyclopentadienyl)-titanium(III) chloride and samarium diiodide at –35 °C results in a colour change from turquoise to deep violet. This colour may arise from a mixture of titanium(IV) complexes, most likely $Cp^*_2TiX_2$ (**53**), and $Cp^*_2TiX(\eta^3$–propargyl) (**54**). Subsequent reduction of **54** by SmI_2 affords the reactive titanium(III) (η^3–propargyl/allenyl) **55** and reduction of $Cp^*_2TiX_2$ by samarium diiodide regenerates the reductive titanium (III) species Cp^*_2TiX **52**. The slow reduction of the alkyl halide to form the organic radical may be induced by samarium diiodide at higher temperatures, or, more likely, through a reaction with Cp^*_2TiX or another adventitious titanium(III) species. The marked absence of other alkylation sites in these compounds makes this process *regiospecific* with respect to radical alkylation.

An interesting study that illustrates the dichotomy of reactivity available to η^3–allyl and propargyl/allenyl ligands to nucleophiles in the rhenium series was designed by Casey.[43] Cationic η^3–allyl rhenium complexes **57** can be accessed by hydride abstraction from the η^2–propene complex **56** using $Ph_3C^+PF_6^-$ (Scheme **1.13**). The propargyl complex **60** is accessed in similar fashion from η^2–2–butynyl rhenium complex **59**. Both allylic and propargyl/allenyl complexes undergo reaction with carbon nucleophiles but with different regioselectivities. The allyl complex **57** is alkylated at one of the terminal carbons to produce elaborated rhenium–alkene complex **58**.[51] In contrast, the propargyl

complex **60** reacts with a variety of nucleophiles at the central position to afford the rhenacyclobutene products **61a** and **61b**.

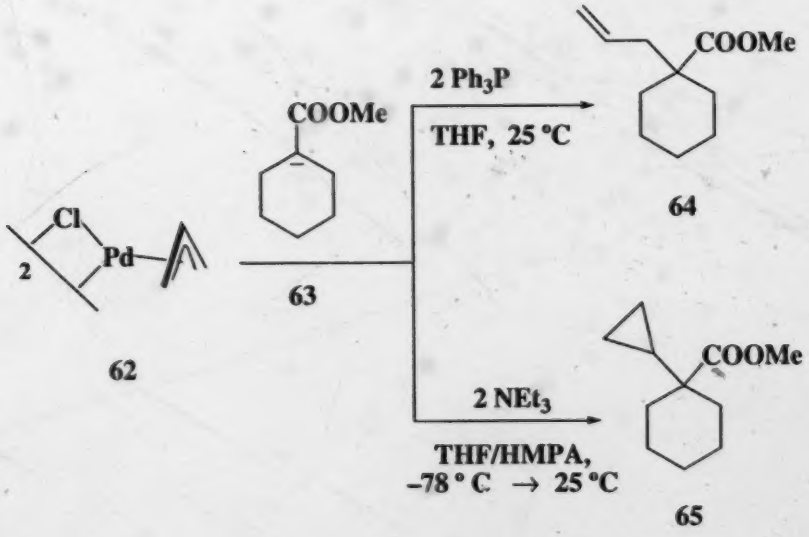
Scheme **1.13**



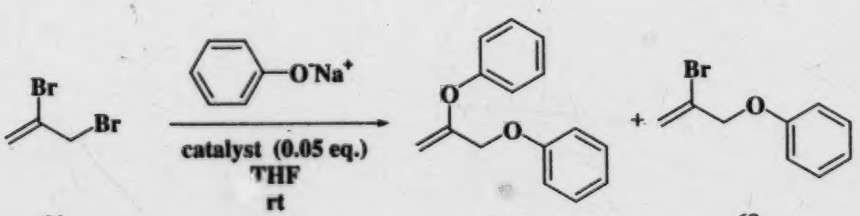
The ability to choose between terminal and central carbon alkylation of π–allyl ligands in organometallic complexes represents an important step forward in understanding these processes. Through judicious choice of nucleophile and by carefully balancing the electronic profile of the metal, different reactive modes can be accessed using Pd(II) allyl complexes. The reaction of palladium π–allyl complexes with stabilized carbanions in the presence of excess phosphine ligand produces elaborated

alkenes.[52] In 1980, Hegedus noticed that in reactions of π–allyl palladium chloride dimer, **62**, the commonly used phosphine ligands could be replaced by HMPA/Et_3N, and still give high yields of terminal alkylation product **64.** [53] However, when relatively nonstabilized deprotonated methylcyclohexylcarboxylate **63** was used as a nucleophile, excellent yields of alkylated cyclopropane **65** were obtained (Scheme **1.14**). Deuterium labelling studies were consistent with cyclopropane formation by nucleophilic attack on the *central* carbon of the π–allyl ligand to form a palladacyclobutane as an undetected reaction intermediate, which reductively eliminates the product cyclopropane. Hegedus found that branched, nonstabilized ester enolates (pKa >20) worked best. Much work has been done in recent years to expand the range of nucleophiles that give central carbon alkylation.[54]

Scheme **1.14**



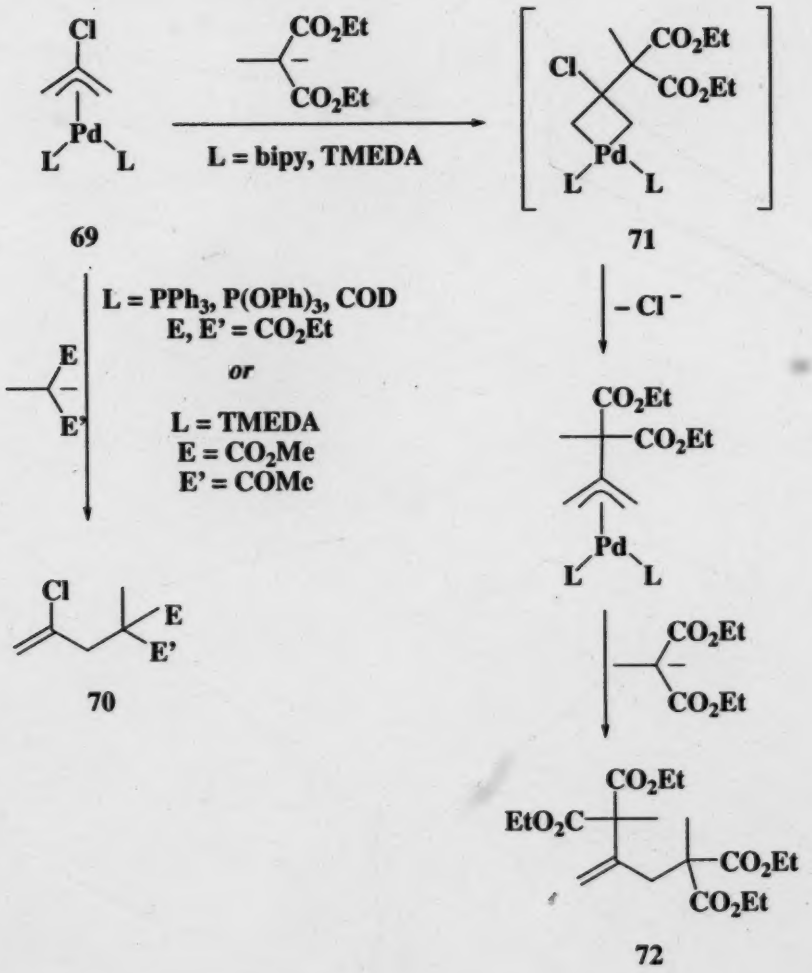
This possibility of terminal versus central carbon addition of palladium π–allyl complexes has been recently exploited and expanded independently by Organ[50] and Bäckvall.[49] In one example, 2,3–dibromopropene **66** was allowed to react with a stabilized anion, sodium phenoxide, in the presence of a catalytic amount of Pd^0.[50] The reaction yields either allylic substitution product **68** or doubly alkylated product **67**, depending on the electronic nature of the ligands used (eq. **1.17**). In the reaction in which the relatively π–acidic triphenylphosphine is employed as the ligand, doubly alkylated **67** is produced exclusively. However, if the pure σ–donor ligand TMEDA is used, the selectivity is completely inverted, furnishing only allylic substitution product **68**. This observation is in sharp contrast to the regioselectivity noted earlier by Bäckvall, who observed that



66 **67** **68** eq. 1.17

alkylation of preformed palladium allyl complexes **69** with diethylmethylmalonate proceeds to give allylic substitution products **70** almost exclusively, despite using π–acidic ligands such as triphenylphosphine, triphenylphosphite, and COD (Scheme **1.15**).[49] With the strong σ–donating bipyridine and TMEDA ligands, a kinetic activity opposite to that observed by Hegedus is reported. Whereas Hegedus reports that the anion of diethylmethylmalonate alkylates π–allyl complexes with σ–donating ligands

Scheme 1.5



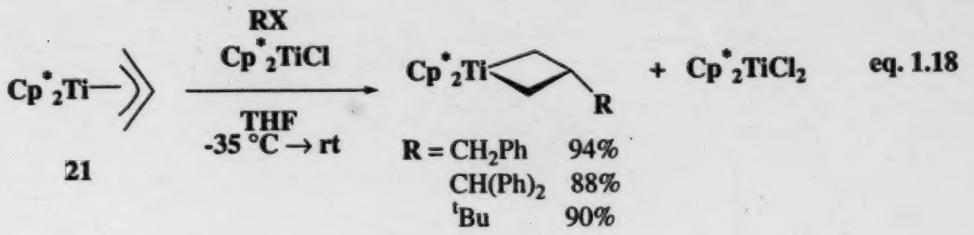
(HMPA/Et_3N) to give elaborated alkene,[53] Bäckvall finds that the anion of diethylmethylmalonate reacts with **69** in the presence of σ–donating ligands (bipy, TMEDA), to afford the doubly alkylated products **72**. This product is thought to be derived *via* a palladacyclobutane[55] intermediate **71** formed by initial nucleophilic attack

of the central carbon. The intermediate **71** ejects chloride anion to reform a π–allyl palladium complex, which then is alkylated by a second equivalent of nucleophile to form the doubly alkylated **72**. However with TMEDA as the ligand and methyl methylacetoacetate anion as nucleophile, only the allylic substitution product **70** was returned. Phosphine ligands with significant electron–donating ability, e.g. dppe, afforded a mixture of products when diethylmethylmalonate anion was used as the nucleophile. The mono–substituted products arise from attack of the terminal carbon of the ligated allyl group. The proposed mechanistic pathway for the doubly alkylated products is shown in Scheme **1.15**.

C. *Radical Generating Strategies: Titanium(III) and Samarium(II)*

Titanium(III) as a radical initiator One of the more difficult and crucial problems to solve in synthetic radical chemistry is that of radical generation/initiation. An early problem that was addressed in the Stryker group was how to generate an alkyl radical with an initiator that is compatible with the reactive, electrophilic titanium(III) and titanium(IV) species present during the course of the reaction. A number of strategies were tested. Titanium(III) compounds are known to act as reductants toward alkyl halides,[56] however bis(pentamethylcyclopentadienyl)titanium(III) chloride worked well only for stabilized or tertiary radicals (eq. **1.18**).

Photolytic decomposition of hexaphenyldistannane in the presence of secondary alkyl halides allows alkylation with secondary radicals;[13] however, this procedure fails



eq. 1.18

for more reactive tertiary and benzylic halides. The common radical initiator, AIBN, proved to be chemically incompatible with the titanium complexes. Although certain approaches worked in certain cases, no one method offered the sort of generality that is required to make this methodology practical until the use of samarium diiodide was evaluated. A powerful one-electron reductant (page 49), samarium diiodide works efficiently and universally within the domain of templates investigated to date to effect clean conversion to titanacyclobutane product. There are other tangible benefits of samarium diiodide methodology as well: the cream–coloured SmX_3 by–products are quite insoluble in THF, largely precipitating out of solution when the reaction is complete, and the products are easily separated from SmX_3 by removal of THF *in vacuo* followed by trituration with pentane, hexane, or benzene.

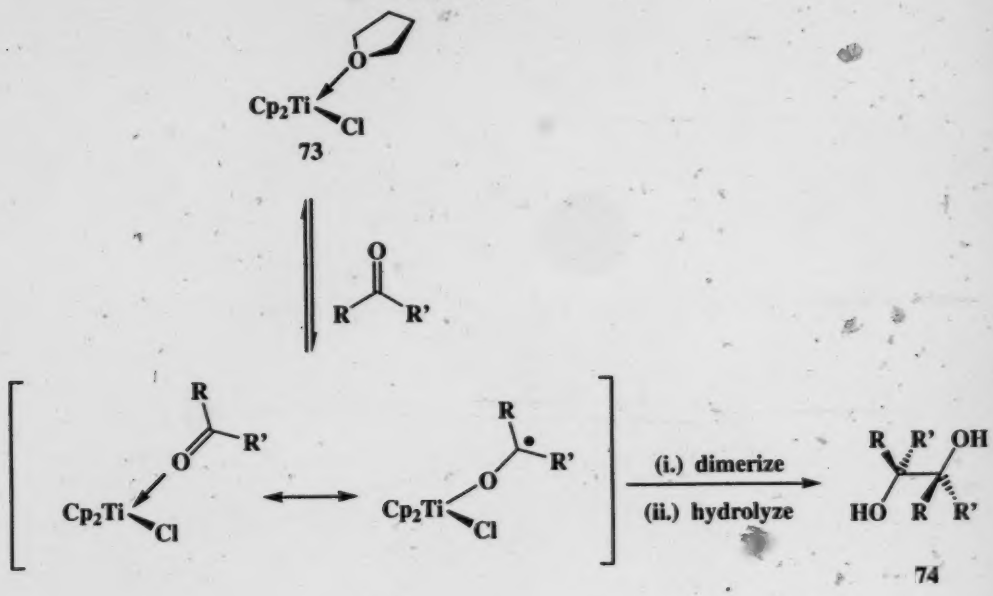
Although the mechanism of radical alkylation of titanocene(III) η^3–ligands using samarium diiodide has not been exactly delineated, observations, control experiments from our group and others, and theory suggest logical mechanistic pathways.[26] Most samarium diiodide reactions in which alkyl halides are reduced require the use of the more reactive alkyl iodide, excess samarium diiodide, and elevated temperatures (>50 °C). The radical alkylations of allyl or propargyl titanium(III) complexes proceed even at

–35 °C in the presence of a stoichiometric amount of samarium diiodide. Because of these observations, and despite the disparity in formal thermodynamic oxidation potentials between Cp^*_2TiCl ($Cp^*_2TiCl^+$// Cp^*_2TiCl 0.14V)[57] and $SmI_2(THF)_n$ (SmI_2^+// SmI_2 –0.98V vs. SCE)[58] or $SmI_2(HMPA)_n$ (SmI_2/HMPA$^+$// SmI_2/HMPA –1.75V vs. SCE),[59] one assumption is that the premier reduction event is the halide abstraction from the propargyl or allyl halide *by titanium* to simultaneously afford the titanium(IV) dihalide and the free organic radical, which then reacts with another equivalent of titanium(III). It is thus clear that our strategy, based on this conjecture, involves the use of titanocene(III) chloride as both the reaction template and the radical initiator, as well as use of samarium diiodide as a radical initiator and/or co–reductant.

The development and application of titanocene catalysts and reagents in organic synthesis is a well–established field.[60] The titanium(III) species Cp'_2TiCl (where Cp' is any substituted cyclopentadienyl ring or cyclopentadienyl itself) is a known one electron reducing agent and has been implicated in a variety of synthetic transformations, including highly diastereoselective pinacol couplings,[61,62] reductive epoxide openings,[63,64,65] synthesis of simple C–glycosides,[66] preparation of glycals,[67,68,69] and reduction of *vic*–dibromides.[70] Inexpensive, commercially available bis(cyclopentadienyl)titanium(III) chloride dimer can be used to reductively couple aromatic and α,β–unsaturated aldehydes to give the corresponding 1,2–diols **74** (Scheme **1.16**).[62] Because the titanium(III) complex **73** is stable to aqueous conditions, the reaction can be run either under anhydrous or aqueous conditions, and because of the templating effect of the ancillary ligands, the pinacol coupling reaction proceeds with

high diastereoselectivity. For example, benzaldehyde is coupled in THF at –78 °C to afford a 98 : 2 dl/meso mixture in 95% yield, or in a 1 : 1 THF/H_2O solvent system at 0 °C to afford a 95 : 5 dl/meso mixture in 89% yield.

Scheme **1.16**

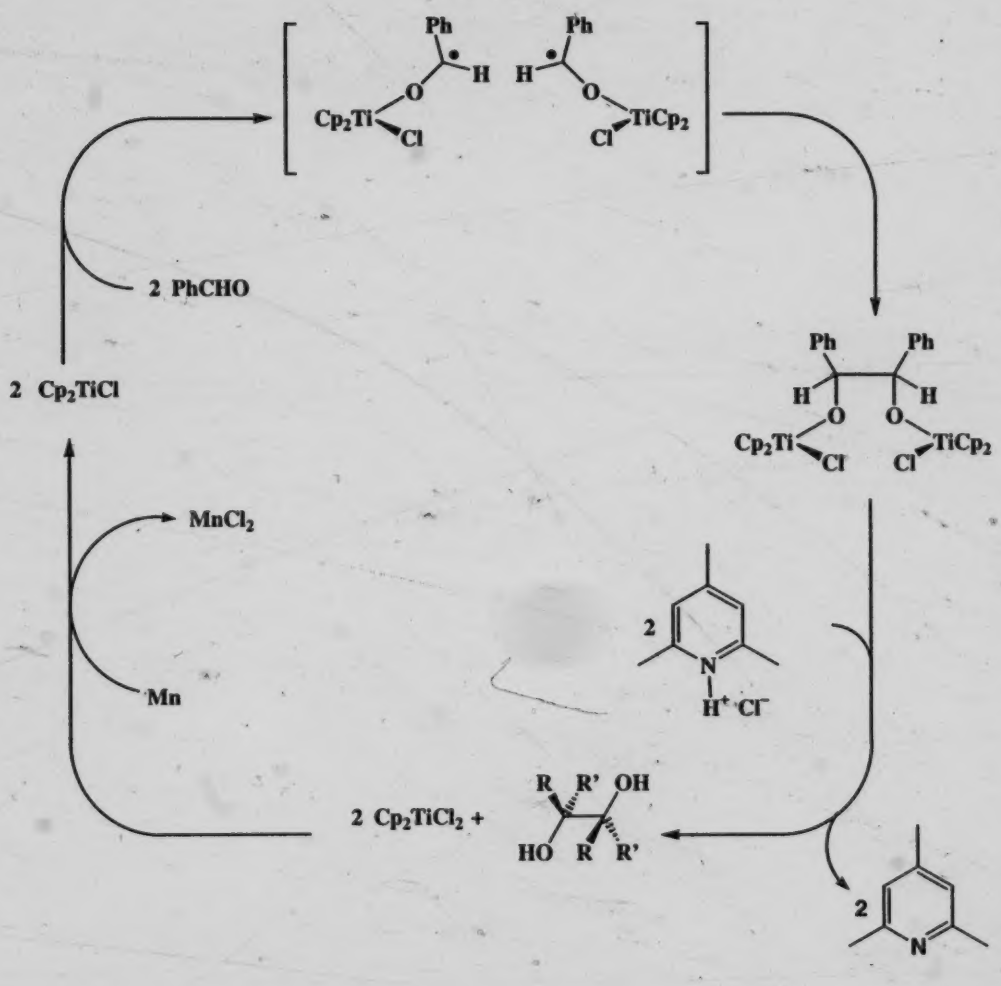


This method of making pinacols was recently rendered catalytic (Scheme **1.17**).[61] In the catalytic sequence, the organic product is demetallated by protonation with collidine hydrochloride, which cleaves the titanium–oxygen bonds to produce the organic product as the *vic*–diol, and converts the bis(cyclopentadienyl)titanium moiety to bis(cyclopentadienyl)titanium(IV) dichloride. Manganese metal is used as a stoichiometric reductant to regenerate the catalytically active bis(cyclopentadienyl)titanium(III) chloride complex. Under optimized conditions, benzaldehyde is coupled in 82% yield with 98 : 2 dl/meso diastereoselectivity using only

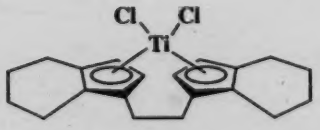
5 mol% of Cp_2TiCl_2. High diastereoselectivities for catalytic pinacol coupling are also observed using Brintzinger's complex,[71] *rac*–ethylenebis(η^5–tetrahydroindenyltitanium) dichloride (EBTHITiCl$_2$) **75**.[61]

Epoxides, valuable and versatile organic synthons readily accessible from alkenes, carbonyl compounds and diols, make excellent radical precursors *via* reductive ring opening mediated by titanocene(III) chloride. The regio– and stereochemistry of epoxide opening by titanocene(III) chloride is guided by the relative stability of the resultant radical,[64b] offering an alternative to the reactivity generated by nucleophilic S_N2–type ring openings, which are typically governed by steric accessibility of the epoxide. The β–titanoxyethyl radicals that result from titanocene–promoted bond homolysis participate in normal radical reactions, such as intermolecular addition to α,β–unsaturated carbonyl compounds.[72] If there is not a suitable organic substrate for the β–titanoxyethyl radical to react with, the radical can be trapped by a second equivalent of titanium(III). 1,2–Elimination of the titanoxy and titanium fragments results in net deoxygenation to yield alkene. In the case of suitably placed unsaturations, such as in 6,7–epoxy–1–heptene **76**, rapid intramolecular 5–exo–trig cyclization[4c,e] of the β–titanoxyethyl radical occurs to form primary alcohol **78** after workup (Scheme **1.18**). In the proposed mechanistic pathway, coordination of the epoxide to titanocene(III) chloride, followed by epoxide opening, creates the transient radical species **77**, which undergoes cyclization onto the olefin moiety.[73] After cyclization, another equivalent of titanium(III) scavenges the primary radical. Quenching of the bis(titanium) complex affords the cyclized product **78** in 70% yield. Recently, Gansauer has rendered this

Scheme 1.17



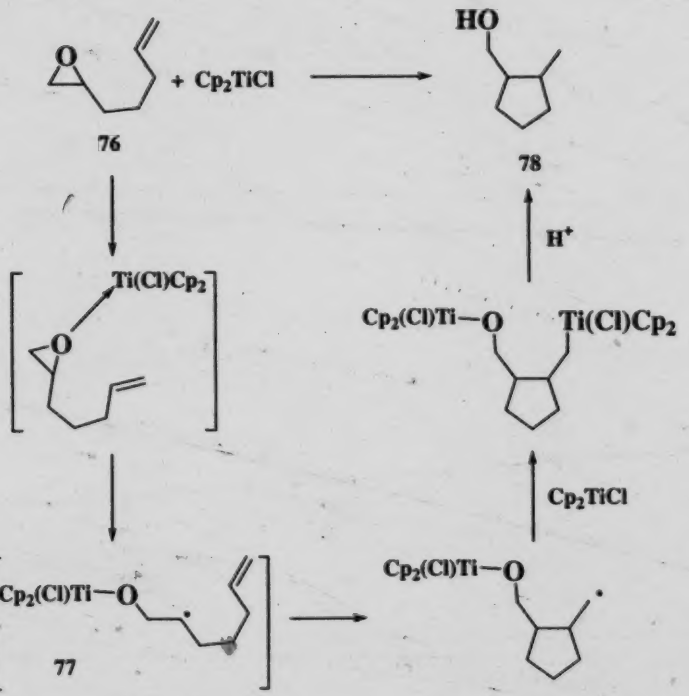
Brintzinger's Compound



75

procedure catalytic as well (Scheme **1.19**).[64a,b] The initial titanium(III)–promoted epoxide opening proceeds as usual.

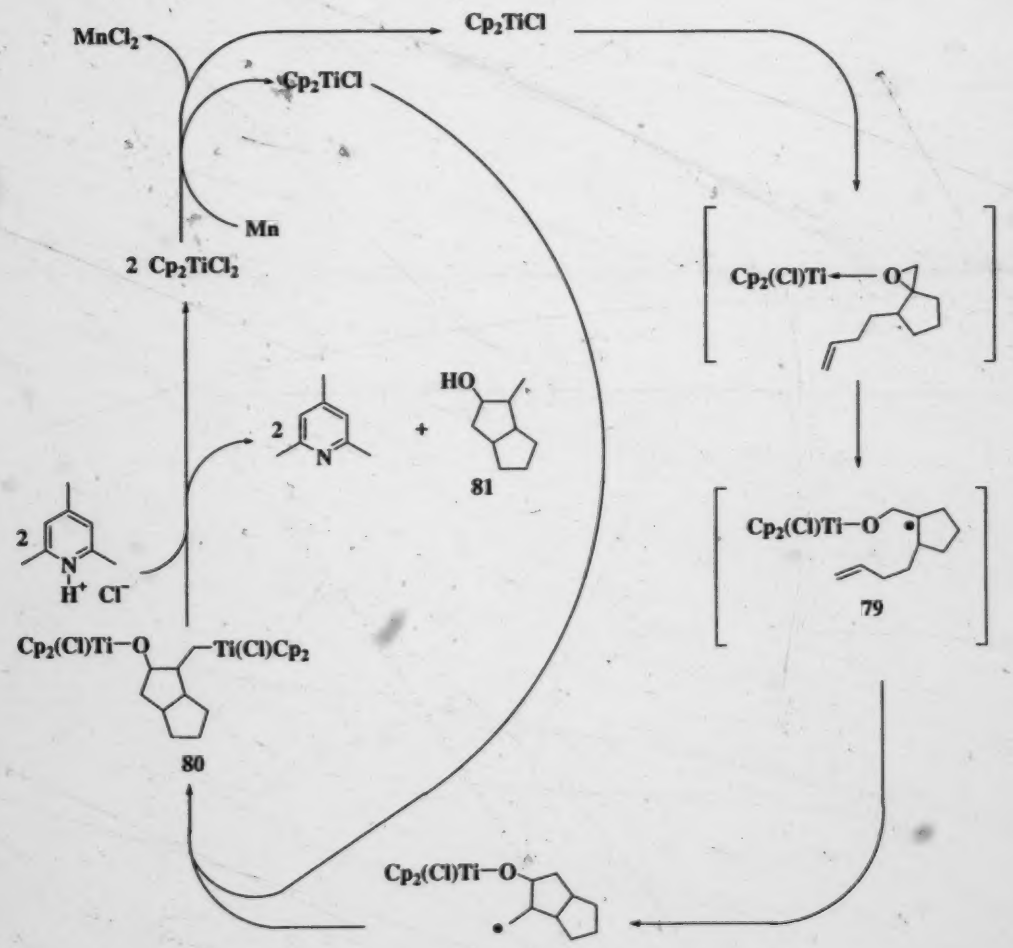
Scheme **1.18**



Following cyclization, the primary radical is formed. Combination with a second equivalent of titanium(III) forms a bis(titanium) complex, which undergoes subsequent protonation of both the titanium–oxygen and titanium–carbon bonds with weak acid to afford the organic product **81**, regenerating the bis(cyclopentadienyl)titanium(IV) dichloride catalyst precursor. The active catalyst, bis(cyclopentadienyl)titanium(III) chloride is regenerated *in situ* by reduction with Mn as a stoichiometric reductant. The

reaction proceeds at room temperature in 66% yield with only 5 mol% of the titanium catalyst.

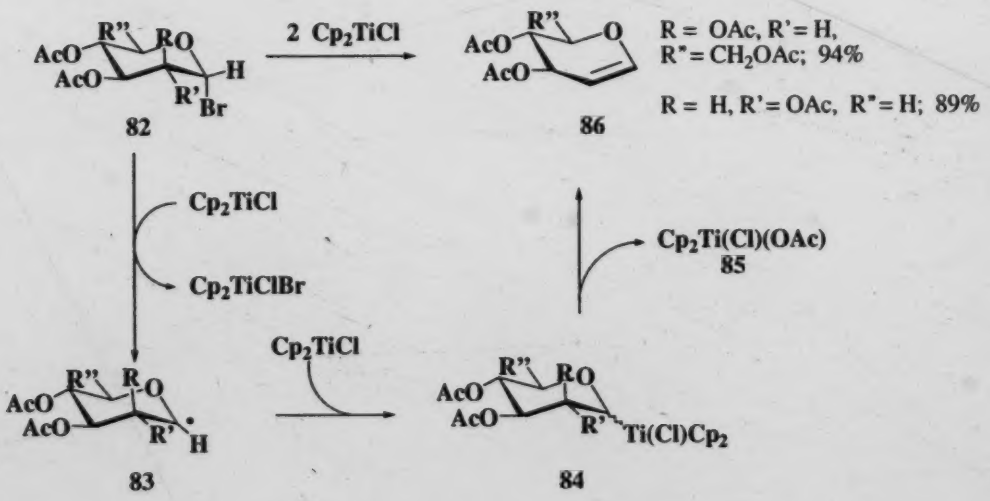
Scheme **1.19**



Synthetically important glycals [74] can be accessed in high yields *via* a similar bis(cyclopentadienyl)titanium(III) chloride–mediated approach.[69] Reductive elimination of acetylated glycosyl bromides to glycals occurs with short reaction times. A wide

range of common carbohydrate protecting groups is tolerated. For example, reduction of the glycosyl bromide **82** with bis(cyclopentadienyl)titanium(III) chloride occurs to afford secondary radical **83**,[75] which is rapidly captured by a second equivalent of titanium(III) to provide the glycosyltitanium(IV) intermediate **84**. Beta–elimination of the C2–acetoxy group as $Cp_2Ti(Cl)(OAc)$ **85** provides the glycal **86** (Scheme **1.20**). In this manner, two equivalents of bis(cyclopentadienyl)titanium(III) chloride are needed per substrate, but a version of this reaction catalytic in titanium has recently been developed.[68] After reductive elimination to form glycal, the titanium(IV) by–product **85** is transformed into bis(cyclopentadienyl)titanium(IV) dichloride by reaction with TMSCl. The catalytically active bis(cyclopentadienyl)titanium(III) chloride is regenerated by *in situ* reduction of bis(cyclopentadienyl)titanium(IV) dichloride with manganese powder.

Scheme **1.20**



The reduction chemistry of titanocene(IV) complexes has been known for a long time. The product of the reduction of titanocene dichloride with sodium[76] and magnesium[77] has itself been used as a powerful reductant.[78] The organometallic product formed from the reaction of bis(cyclopentadienyl)titanium(IV) dichloride and magnesium for example, reduces alkyl organic chlorides and bromides, aryl bromides, and azo compounds in good yields.[79] The reduction of organic halides proceeds at 0 °C. The active reductant formed is assumed to be d^2–titanocene. Odd–electron bis(cyclopentadienyl)titanium(III) chloride, formed from the *in situ* reduction of bis(cyclopentadienyl)titanium(IV) dichloride with isopropylmagnesium halide[78a] or Al^0,[80] is effective in the dehalogenation of benzylic and allylic halides and α–bromoketones. Benzylic and allylic halides are transformed into dimerized products, whereas the α–bromoketones are reduced to the corresponding ketones. Under similar conditions, $PhCH_2CH_2Cl$, EtBr and PhBr fail to react with bis(cyclopentadienyl)titanium(III) chloride.

Samarium (II) as a radical initiator. Twenty–four years have passed since the introduction of samarium diiodide as a reagent for organic synthesis by Kagan and coworkers.[81] Samarium diiodide is most widely used as a solution in THF,[82] and exists as a monomer[83] in THF solution with several THF molecules acting as ligands.[84] That samarium diiodide is a versatile reagent for organic synthesis is demonstrated by its ability to mediate a wide array of single–step and sequential reactions *via* both radical and formally anionic processes.[85] The importance of this methodology is attested to by

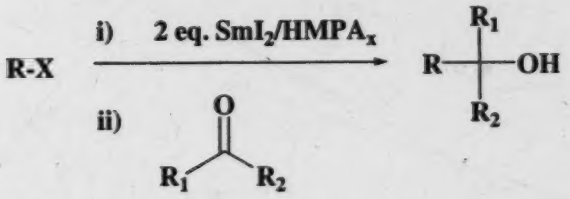
the number of syntheses in which it has been used[86] and by the number of reviews this highly popular reagent has engendered.[86,87] Samarium diiodide promotes an assortment of useful organic reactions, including radical cyclizations, ketyl–alkene coupling reactions, pinacol couplings, conjugate additions,[85] and coupling of organic halides with carbonyl compounds (Barbier/Grignard–type reactions).[86a,87a] Seminal work by Kagan[81,88,89,90] served to outline the utility of samarium diiodide in intermolecular Barbier reactions, as well as deoxygenations of epoxides and sulfoxides.[91] He noted that functional groups such as double bonds and alkyl bromides remain intact upon exposure to a THF–MeOH solution of samarium diiodide, while cinnamic acid and its methyl ester are quantitatively reduced to the saturated acid and ester, respectively. Aliphatic aldehydes can be selectively reduced in the presence of a ketone.[81] Kagan established for the first time the formation of tertiary alcohols from the reaction of alkyl halides and ketones in the presence of samarium diiodide in THF solution; the now–named samarium Grignard (SGR) and samarium Barbier reactions (SBR)[81] (Scheme. **1.21**). In the original experiments, three equivalents of a halomethane or haloethane per equivalent of samarium diiodide and an aliphatic ketone or aldehyde[92] were allowed to react in THF at reflux (Table **1.5**). Kagan found that iodoethane is more reactive than bromomethane and that when the ratio of SmI_2 to substrate is increased, better yields of addition product are obtained. These initial results have inspired much work in the field of SBR and SGR reactions.[86a]

Especially when complexed with HMPA, SmI_2 is a remarkably powerful and selective reductant. Although in the absence of HMPA primary halides are slow to

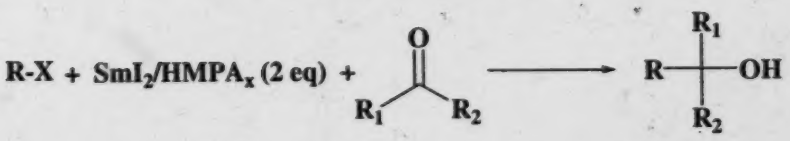
reduce,[93] with HMPA, primary, secondary, and tertiary halides are reduced efficiently to the corresponding alkane even under very mild conditions and in the presence of other functional groups.[94] In general, alkyl iodides and bromides react much more quickly than chlorides.

Scheme **1.21**

Samarium-Grignard Reaction (SGR)

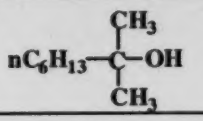
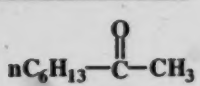
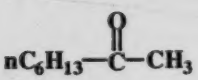
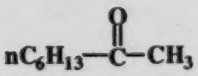
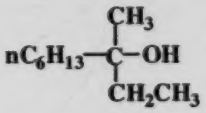
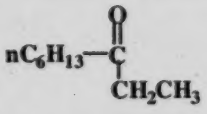
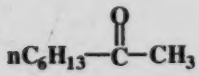
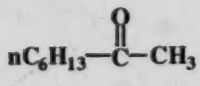


Samarium-Barbier Reaction (SBR)



Substantial differences are noted in the reactivity of SmI_2 with alkyl halides and tosylates compared to allylic, benzylic, and propargylic halides. Whereas in THF at reflux primary bromides, iodides, and tosylates are reduced to hydrocarbons in high yields, benzylic or allylic halides provide high yields of radical coupling products even at room temperature.[91] No coupling products are detected in the reactions with primary halides. This difference has been ascribed to differences in the stability of the radical. Alkyl

Table 1.5 Products of the SGR and SBR reactions

substrate	alkyl halide	ratio Sm:substrate	product, yield (%)	
				
	CH_3I	2	(70)	(30)
	CH_3I	3	(95)	(5)
				
	CH_3CH_2I	2	(70)	(30)
	CH_3CH_2Br	2	(60)	(40)

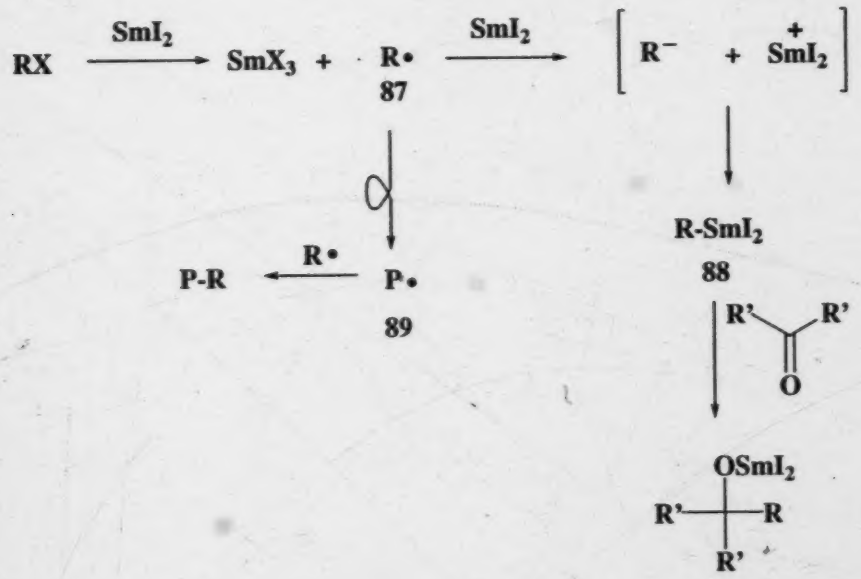
radicals are reduced rapidly to the organosamarium compounds, which are inert to coupling, and ultimately quench to yield alkane. Stabilized benzylic and allylic radicals are more persistent, and survive long enough to undergo radical–radical coupling.[95] The SmI_2(HMPA) complex also reduces vinyl and aryl halides under mild conditions, but require slightly longer reaction times than for reduction of the alkyl halides.

Mechanistic studies of the samarium diiodide–promoted reduction of alkyl halides and tosylates to alkane initially suggested a radical mechanism for the reduction step.

Alkyl halides react with samarium diiodide in THF solution at reflux, but the absence of deuterium incorporation into the products upon quenching with deuterated water suggested that the reductions do not go through an "anionic" organosamarium intermediate.[96] Instead, the formation of a free radical was proposed, and H–atom abstraction from the THF solvent was speculated to lead to alkane product.[97] More recently, the reduction of primary and secondary alkyl halides by samarium diiodide and SmI_2(HMPA) has been evaluated in detail to help understand the nature of samarium Grignard/samarium Barbier reactions.[95] Curran critically evaluated the existing evidence, provided some new evidence, and proposed some mechanistic direction concerning the alkyl halide reduction. In this mechanistic work using the SmI_2(HMPA) system, the reaction was conducted under milder conditions, and produced deuterated product upon quenching with deuterated water.[96] To explain the result, the authors invoke an organosamarium intermediate and suggest that in the prior experiments the non–deuterated product arose not from radical processes but from the decomposition of the organosamarium intermediate at reflux temperatures. A mechanistic sequence for these types of reactions was proposed (Scheme **1.22**): the first reduction event concurrently creates free radical[95] **87** and SmX_3 by simultaneous electron transfer and C–X bond homolysis.[98] The organic radical then can experience a number of fates: in the presence of a suitable radicophilic moiety, it undergoes reaction to create a new radical **89**, which then undertakes normal radical processes. Alternatively, the radical **87** can be further reduced by a second equivalent of samarium diiodide to give an organosamarium species **88** that undergoes 1,2 addition with a ketone. The relative rates of these competitive

processes have been evaluated.[93] Primary and secondary radicals are reduced to organosamarium reagents, but tertiary radicals are not.[95,99,100]

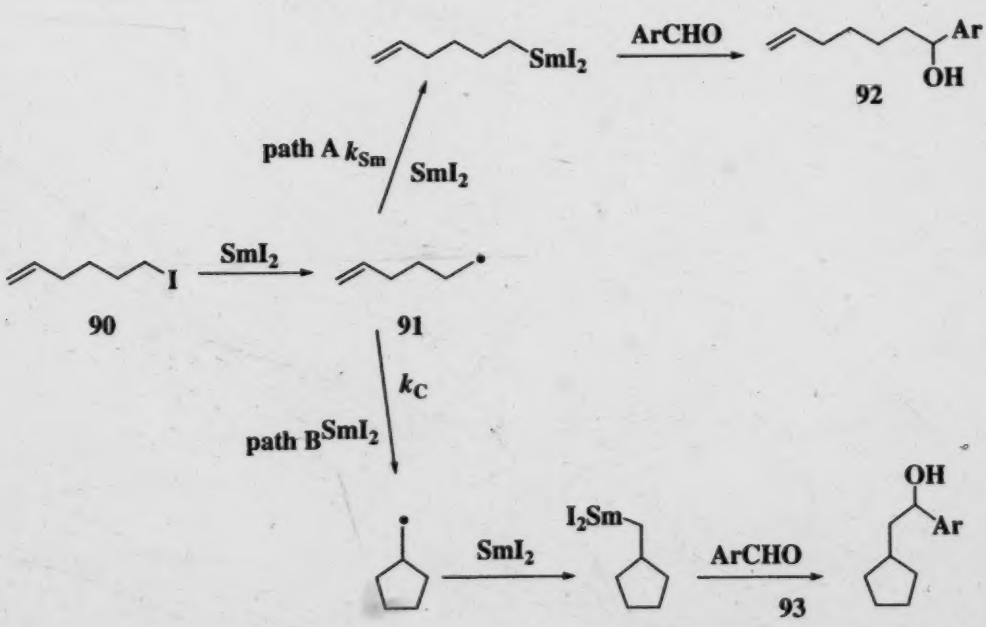
Scheme **1.22**



Curran proposed that primary alkyl radicals[101] and samarium diiodide combine directly *via* inner–sphere electron transfer to form the organosamarium species without the formation of a discrete anionic species.[95] Flowers, however, showed that primary alkyl radicals are reduced *via* an outer sphere mechanism to give carbanions and therefore must exist for some finite time as a discrete entity.[59] The second reduction is fast: the intermolecular reduction by samarium diiodide (path A) (Scheme **1.23**) is competitive with intramolecular 5–exo–trig cyclization (path B).[93] The resulting "free" anion combines with the SmX_2^+ cation to form the observed organosamarium species. The

same study[59] also ruled out inner–sphere electron transfer to alkyl and vinyl halides, suggesting that unless the species to be reduced is nucleophilic enough to displace the strongly bound THF or HMPA ligands, the reduction event will probably occur by an outer sphere process. Benzyl bromide, for example, was specifically shown to react by an outer–sphere electron transfer.[59,100]

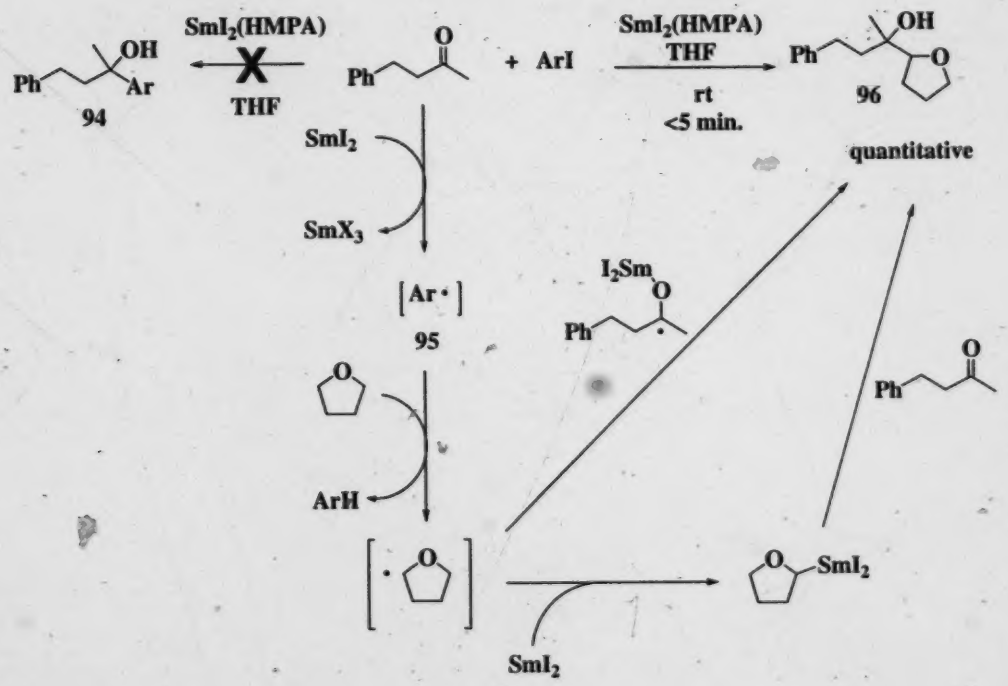
Scheme **1.23**



Vinyl and aryl radicals have a very short lifetime in THF, and reactions that use the SmI_2(HMPA) reagent to generate them are limited largely to intramolecular processes. Attempts to perform intermolecular chemistry are generally frustrated by H–atom abstraction from THF. For example, the attempted SmI_2(HMPA)–mediated coupling of an aryl iodide and a ketone produced none of the desired SBR coupling

product **94**, but quantitatively produced tetrahydrofuran addition product **96** after quenching (Scheme **1.24**).[102] The authors speculate that the solvent becomes a radical scavenger: aryl radical **95**, formed by reduction of the aryl iodide, reacts with THF before it is able to couple with the ketone. The resultant *tetrahydrofuranyl* radical either couples with a samarium

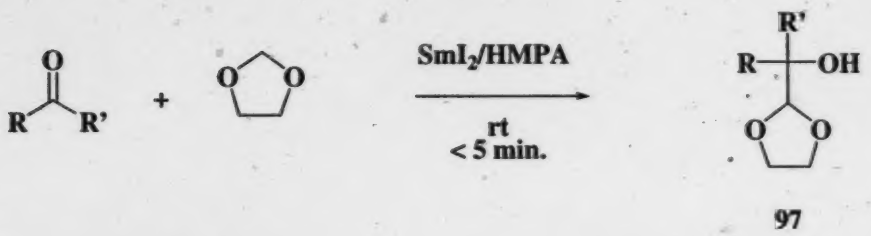
Scheme **1.24**



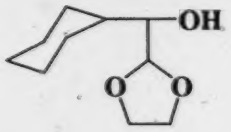
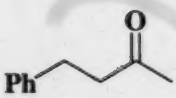
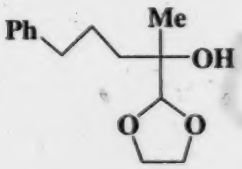
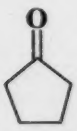
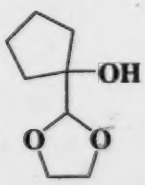
ketyl complex or becomes reduced to the organosamarium reagent, which then couples with the ketone to form **96**.[95] This facile H–atom abstraction from THF has been exploited by Inanaga in a new method for synthesizing masked formylated–carbonyl compounds.[102] Replacing THF with 1,3–dioxolane allows for the formation of masked

α–hydroxy aldehydes **97** (Scheme **1.25**). The reactions require five equivalents of PhI and six equivalents of samarium diiodide per equivalent of carbonyl compound.

Scheme **1.25**



97

carbonyl compound	product (% yield)	
cy-CHO		(73)
		(73)
		(76)

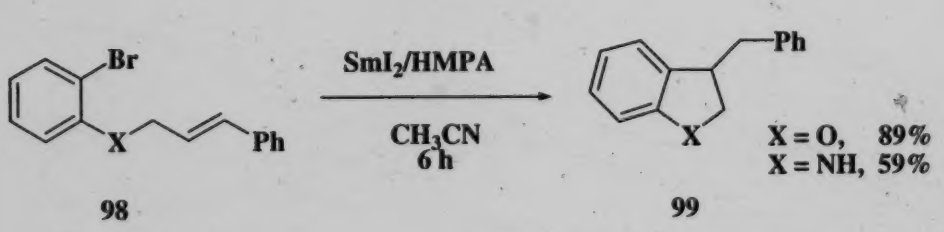
From the early stages of the development of samarium diiodide as a synthetic reagent, the more strongly reducing $SmI_2(HMPA)_n$ complex was recognized as a way of promoting reactions that are otherwise slow. For example, Curran employs 6–iodo–1–hexene **90**, as a radical clock[103] to study the mechanism by which primary alkyl halides react in samarium diiodide solutions.[93] The 6–hexenyl radical is well–studied, and the rate

constant for its 5–exo trig closure has been determined to be $k_C = 10^5\ s^{-1}$.[104] Because of its known rate constant, it is used as a "radical clock" to determine the rate constants for primary radical processes.[105,106] In samarium diiodide solutions with no HMPA, the reaction of 6–iodohexene **90** at room temperature was on the order of "several hours to one day." However, with the addition of as little as two equivalents of SmI_2(HMPA), reaction times were reduced to minutes.[93] By assessing the product distribution from the reaction, hypotheses can be drawn about the relative contributions of radical and anionic processes (see Scheme **1.22**, page 54). The product distribution varied with the amount of HMPA present. With more HMPA, the amount of intermolecular addition product **92** (path A), increased until the ratio of HMPA:SmI_2 reached ~4:1. A negligible difference in product ratio is observed at ratios > 4:1, suggesting that the maximum coordination number of HMPA ligands in THF solution is four. The experiment demonstrates that as the number of HMPA ligands increases, the rate of reduction of organic radical **91** increases, thus increasing product derived from path A. The relatively equal formation of **92** and **93** from the reaction employing four equivalents of HMPA demonstrates that the rate constant of the intermolecular reduction is similar to the rate constant of intramolecular cyclization of **91**. The increased oxidation potential of the SmI_2(HMPA) complex enhances the reduction rate by better facilitating electron transfer. The structure of SmI_2(HMPA) complex has been determined for the solid state,[107] and postulated for the solution state. In solution, SmI_2 tightly coordinates four HMPA ligands.[83] The effect of this ligation is to substantially lower the peak potential of the [SmI_2// SmI_2^+] couple (*vide supra*). The versatility of SmI_2 as an organic reagent is furthered by the ability to

modulate reactivity by use of external catalysts,[108] through solvent effects,[93,100b,109] or by altered reaction conditions.[85] Other ligands that alter the oxidation potential of SmI_2 have been studied,[109] many of which offer a much less toxic alternative to HMPA.[110] These include DMPU,[111,112,109,113,114] water,[113] triethyl amine,[115] lithium halides,[116] metal salts,[108] Sm powder,[117] and visible light.[118]

Although SmI_2 efficiently reduces alkyl halides, the reduction of vinyl halides is not as general, and while subsequent reduction of alkyl radicals to organosamarium reagents is a facile process, evidence of the corresponding reduction of vinyl radicals has only been claimed under certain special circumstances.[119,120,121,122] In general, the reactive vinyl or aryl radical reacts quickly either by H–atom abstraction from the solvent[102] or by addition to a suitably placed radicophilic moiety, as in intramolecular cyclizations[4b] onto double or triple bonds.[95,123,124] Inanaga has constructed furan and indole compounds by employing the latter strategy.[125] Aryl halides **98** undergo reduction using SmI_2(HMPA) in THF solution at room temperature. Cyclization onto the proximal unsaturation generated the bicyclic derivatives **99** (Scheme **1.26**).

Scheme **1.26**



98 **99**

Chapter 2. ***Free Radical Alkylation Of Ti(III) Propargyl Complexes. Regioselective Inter– and Intramolecular Central Carbon Alkylation to Form Substituted Titanacyclobutene Complexes.***

A. Intermolecular Free Radical Alkylation Reactions.

There are relatively few methods of generating titanacyclobutene complexes, and fewer still of generating them with full regiocontrol of the ring substituents. This chapter describes our attempts to expand the scope of titanacyclobutene complex synthesis *via* radical alkylation methodology through the application of various substrate types, and consequently expand the types of titanacyclobutene complexes that can be prepared.

Of the classes of titanacyclobutene complexes existing in the literature, all possess cyclopentadienyl or cyclopentadienyl–type ligands as the ancillary ligand set, and can therefore be classed generally as "titanocenes." The most common method for generating titanacyclobutene complexes is by the reaction of an alkyne with some *in situ*–generated titanocene –methylidene,[126,127,179] –alkylidene,[128] or –vinylidene[129,130,131] compound. The resulting [2+2] cycloaddition affords a titanacyclobutene complex, usually in good yield. There is little control over the alignment of the alkyne with the titanium methylidene fragment in the transition state, resulting in a distribution of regioisomers.[130a,131] Symmetrical alkynes are usually used to avoid the generation of regioisomers with the obvious drawback that the target titanacyclobutene compound must have two identical substituents that originate from a symmetrical alkyne. If an unsymmetrical alkyne is employed, a low yield of the desired product is suffered due to

the mixture of regioisomers. As well as affecting reaction yields, this method clearly results in limitations in structural diversity. Additionally, terminal alkynes are not generally tolerated. Titanacyclobutene intermediates would clearly be of greater use synthetically if regioselective incorporation of ring substituents were possible.

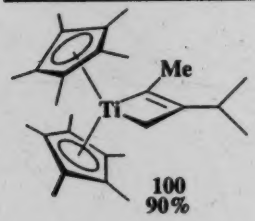
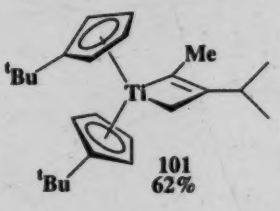
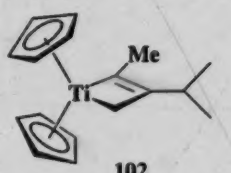
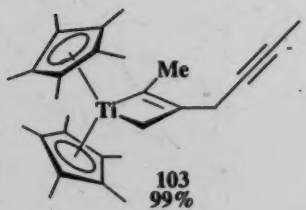
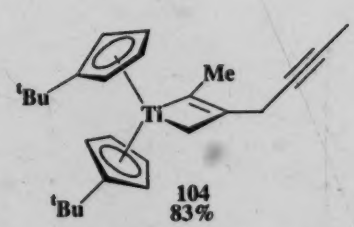
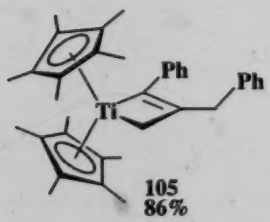
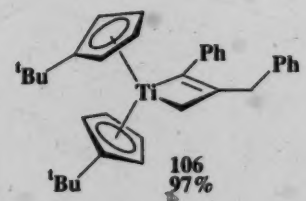
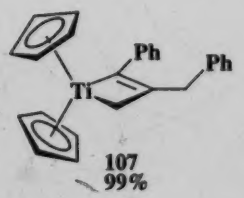
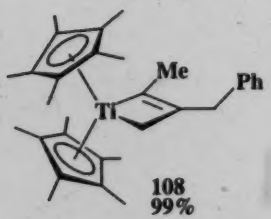
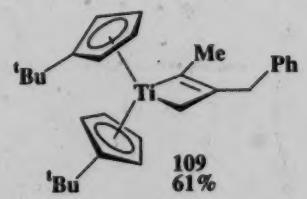
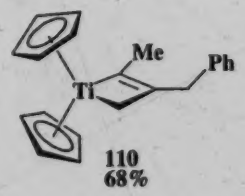
Almost all of the reduction reactions of alkyl halides in the literature involving samarium diiodide employ at least two equivalents of the samarium reductant per reduced halide (see Scheme **1.23**, pg. 55). These procedures have been developed based on two-electron processes, probably involving two discrete single-electron transfer (SET) steps..[132,133] In the samarium diiodide–mediated formation of titanacyclobutene complexes, the sequence of reactions is likely different; the alkyl halide is probably not transformed into a samarium Grignard reagent. Under the mild conditions of titanacyclobutene complex synthesis, we purport that there is initially formed a η^3–bound propargyl fragment occupying two coordination sites on the titanocene(III) "template". There is crystallographic evidence to support this assertion.[19,29] As previously discussed, it is unlikely that the propargyl moiety is loaded onto the titanium centre *via* an organosamarium intermediate under the standard conditions for titanacyclobutene complex synthesis, which involve adding both the propargyl halide and alkyl halide at -35 °C to a solution containing only one equivalent of samarium diiodide per propargyl and alkyl halide. At this temperature [86a] and with this stoichiometry of samarium diiodide, a free-radical pathway is considered to be more likely. For the same reasons, and because only one equivalent of SmI_2 remains after propargyl complex formation, it is probable that it is a carbon–based radical (as opposed to an organosamarium reagent) that

combines with the η^3–bound propargyl fragment to form the titanacyclobutene product. Carbon radical combination with the titanium propargyl complex occurs at the slightly bonding SUMO (Fig. **1.5**, page 29), whereas an anionic process would involve attack at the antibonding LUMO. It remains possible, however, that the alkylation event occurs through the intermediacy of a carbon–based anion. The radical anion formed from the addition of an anionic samarium Grignard reagent to the titanium(III) complex could transfer an electron to the intimately–coordinated SmX_2 radical cation, thus regenerating the SmX_2 reductant.

Encouraged by the success of regioselective radical alkylation of η^3–allyl titanium(III) complexes to form titanacyclobutane complexes,[13] workers in the Stryker group successfully extended this technology to the corresponding η^3–propargyl system. Radical additions proceed at the central carbon to afford the expected titanacyclobutene complexes, with full regiocontrol. Some results using the bis(pentamethylcyclopentadienyl)titanium(III) chloride system have been reported (see Chapter One eqs. **1.11**, **1.12**, and Table **1.2**), and are shown in Table **2.1**, column **1**.[19] Provided this methodology can be coupled with small molecule insertion chemistry, it can provide a powerful strategy for rapidly elaborating molecular complexity.

Upon demonstrating that central carbon radical alkylation of titanium(III) propargyl compounds can be accomplished, the logical second phase of this inchoate methodology is expansion to one of a more generally useful nature. This requires that propargyl halides and alkylating radicals bearing diverse functional groups be tolerated

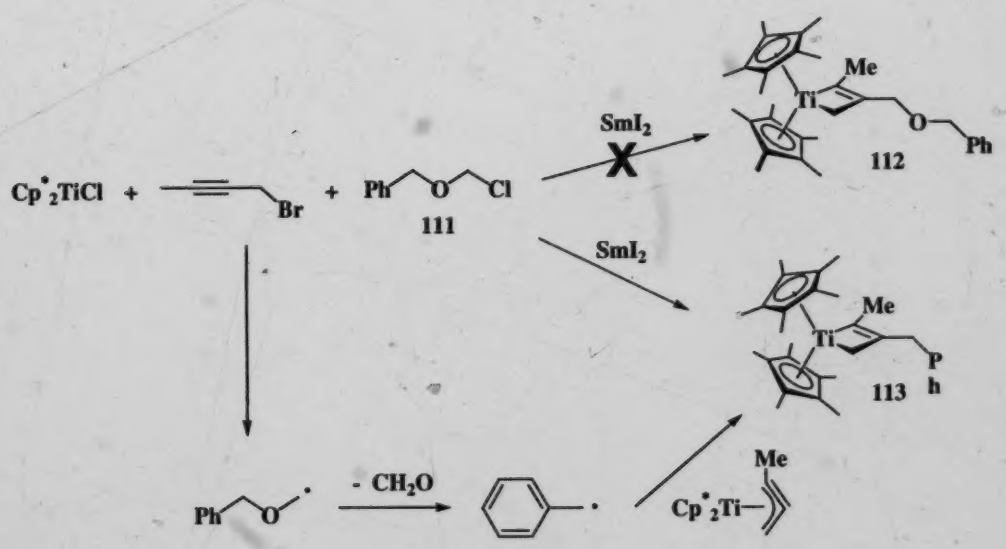
Table 2.1 Some titanacyclobutene complexes prepared by radical alkylation reactions

Cp*[19]	^{t}BuCp	Cp
 100 90%	 101 62%	 102 85%
 103 99%	 104 83%	
 105 86%	 106 97%	 107 99%
 108 99%	 109 61%	 110 68%

by the metal species and not undergo destructive side reactions. Attempts to incorporate a heteroatom such as oxygen into the incoming organic radical fragment have, however,

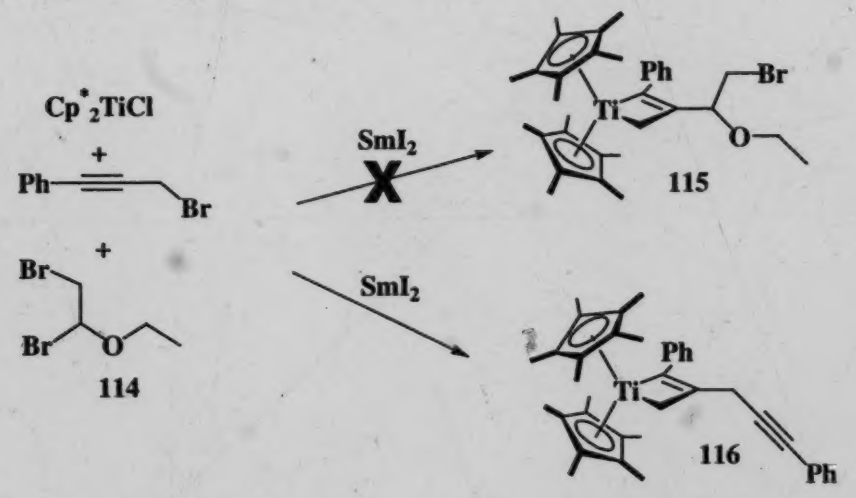
met with only limited success. For example, the attempted synthesis of titanacyclobutene compound **112** by the standard procedure using benzyloxymethyl chloride **111** as the alkylating radical source led instead to the unexpected benzyl β–substituted titanacyclobutene **113** in moderate yield (Scheme 2.1).[29] An extrusion of formaldehyde following the initial reduction of **111** is speculated to occur, with benzyl radical ultimately acting as the alkylating agent. Also attempted was the use of 1,2–

Scheme **2.1**



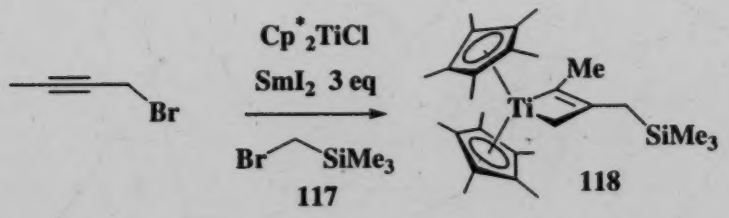
dibromoethyl ether **114** as a radical source (eq. **2.1**). Instead of the anticipated titanacyclobutene product **115**, propargyl adduct **116** was obtained as the only product in low yield. The first example of successful heteroatom inclusion into the titanacyclobutene complex product was from the use of bromomethyltrimethylsilane **117**

as a radical source, which produces titanacyclobutene complex **118** in high yield (eq. 2.2).[29]



eq. 2.1

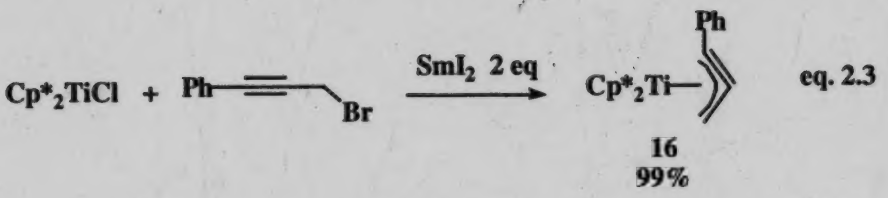
Qiu also reported the only example of heteroatom incorporation into the propargyl fragment. When 3–bromo–1–phenylpropyne was allowed to react with bis(pentamethylcyclopentadienyl)titanium(III) chloride and samarium diiodide, the stable



eq. 2.2

93%

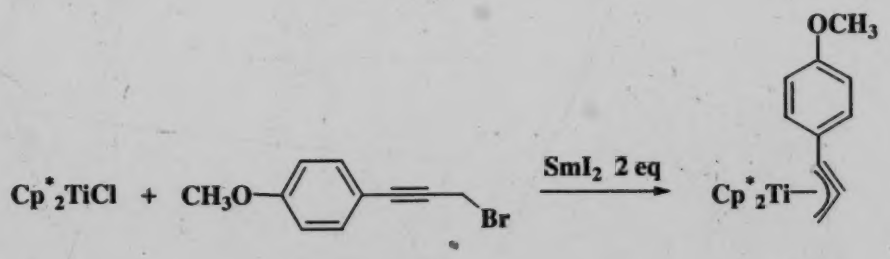
η^3–propargyl/allenyl titanium (III) species **16** was isolated in high yield (eq. **2.3**).[19] Although quantitative dimerization was seen in the unsubstituted propargyl case,[19] no



16
99%

eq. 2.3

dimerization of **16** was detected. In an effort to further understand the nature of the η^3–propargyl complexes that are the putative intermediates in the titanacyclobutene complex formation, the same reaction using 1–(4–methoxyphenyl)–3–bromopropyne **119** (eq. **2.4**) was attempted. It was anticipated that the increase of electron density over



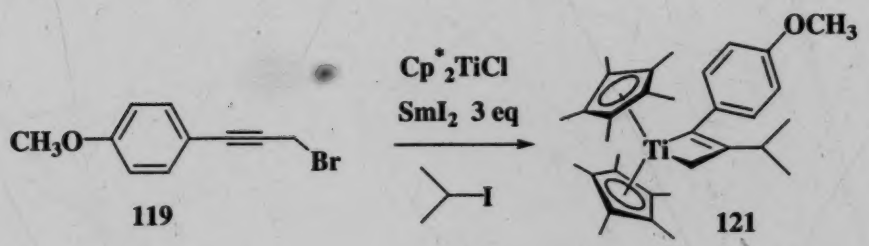
119 120

eq. 2.4

3–bromo–1–phenylpropyne might allow for ligand–ligand dimer formation. In the event, no dimerization products were detected. Compound **120**, however, proved to work well in standard intramolecular radical alkylation reactions. For example, compound **121**, with incorporated heteroatom, is formed by the general reaction procedure in high yield (eq. **2.5**).

In general, varying the ancillary ligand set between pentamethylcyclopentadienyl, *tert*–butylcyclopentadienyl, and cyclopentadienyl in the template affects yields somewhat, but does not change the overall reaction pattern (see Table **2.1**, pg. 63). The

more electron-rich pentamethylcyclopentadienyl ligand set gives better yields. There is a general trend towards lower yields as the ancillary ligand is changed to the less electron-rich *tert*–butylcyclopentadienyl and cyclopentadienyl ligand sets. This is offset by the greater ability to functionalize the titanacyclobutene products in the *tert*–butylcyclopentadienyl and, in particular, the cyclopentadienyl series of complexes.



eq. 2.5

i. Substrate synthesis

A series of experiments was performed to extend this reaction to new combinations of propargyl substituent and radical addend. Commercially available propargyl halides 1–bromo–2–butyne and 3–bromo–1–phenylpropyne were purified by passing through neutral alumina, and then degassed by consecutive freeze–pump–thaw cycles under high vacuum ($< 10^{-5}$ torr). Radical precursors iodomethane, diiodomethane, dibromomethane, and 2–iodo–propane were purified in the same way. Commercially unavailable substrates were synthesized.

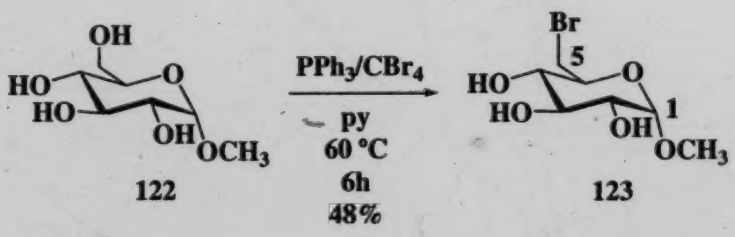
In an attempt to expand the number of heteroatom–containing substrates compatible with the formation of titanacyclobutene complexes, several synthetically

useful classes of molecules were considered. Simple sugars can be easily manipulated by known reactions, and if successfully employed as substrates in titanacyclobutene complex–forming reactions, could provide a potentially interesting class of molecules: carbohydrate–substituted titanacyclobutene complexes which presumably can be regarded as useful starting materials for a number of synthetic transformations. Incorporation of a sugar moiety into the titanacyclobutene structure potentially provides a new method for functionalizing carbohydrates. Common starting material methyl α–D glucopyranoside **122** was chosen for the study because it is readily available, and possesses a primary hydroxyl group that can be easily converted to a bromine atom. The primary bromide group can serve as a radical source, and sugars possessing this group are potential radical precursors for titanacyclobutene complex synthesis. Carbohydrate substrates methyl 6–bromo–6–deoxy–D–glucopyranoside **123**, and methyl 2,3,4–tris–O–benzyl–6–bromo–6–deoxy–D–glucopyranoside **126** were prepared from methyl glycoside **122**.

Radical precursor methyl 6–bromo–6–deoxy–D–glucopyranoside[134] **123** was constructed by transformation of the 6–hydroxy group of methyl α–D glucopyranoside to a bromine atom (eq. **2.6**). Selective transformation of the primary alcohol to bromide was achieved in one step using PPh_3/CBr_4.[135] The target material **123** was recovered as a white crystalline solid in 48% yield after recrystallization from boiling acetone.

The anomeric hydrogen (H1) appears as a doublet in the ^1H NMR spectrum at δ 4.64. H5 appears as a doublet of doublet of doublets at δ 3.64, and the diastereotopic

hydrogens at H6 each appear as a doublet of doublets. Spectroscopic data is consistent with published results.

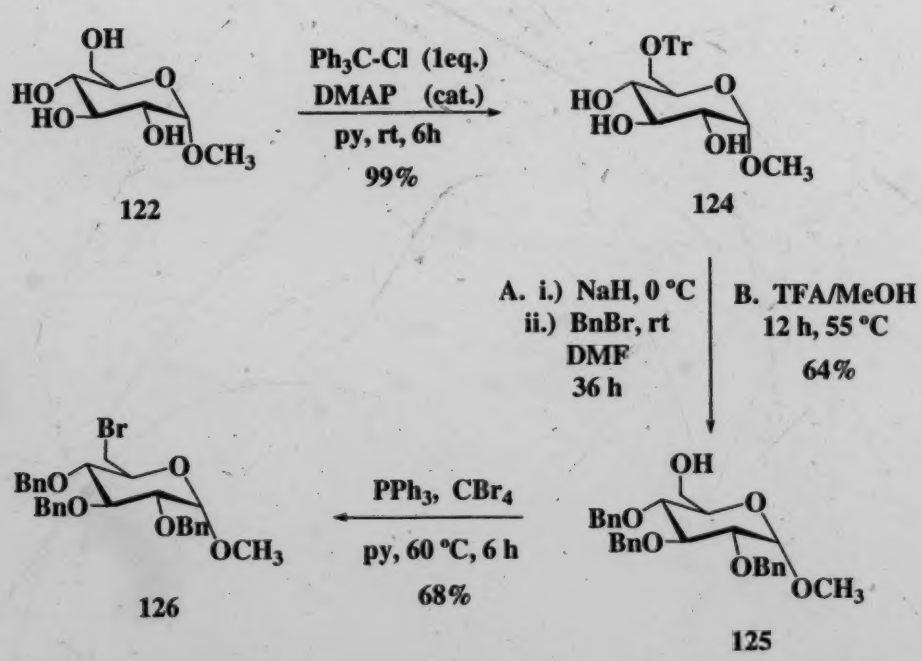


eq. 2.6

The fully protected sugar methyl 2,3,4–tris–O–benzyl–6–bromo–6–deoxy–D–glucopyranoside[136] **126** was also constructed from methyl α–D glucopyranoside **122** (Scheme **2.2**). Protection of the secondary hydroxyl groups as the benzyl ethers required prior protection of the primary hydroxyl group at C6 of methyl glycoside **122** as the triphenylmethyl (trityl) ether. Tritylation was accomplished in high yield with triphenylchloromethane and a catalytic amount of DMAP in pyridine.[166] The base–stable trityl species **124** can then be benzylated under standard conditions. Thus, the protected sugar was dissolved in DMF, cooled to 0 °C, and treated with an excess of sodium hydride and benzyl bromide to give the crude fully protected sugar. This material was dissolved in a 1:1 mixture of trifluoroacetic acid and methanol and heated to reflux to remove the triphenylmethane protecting group. Tribenzyl protected sugar **125**, with a free C6 hydroxyl group, was recovered as a white solid after silica gel column chromatography (dichloromethane eluent). The primary hydroxyl group on sugar **125** was transformed to bromine using PPh_3/CBr_4 in pyridine,[135] producing the desired protected sugar **126** in 68% yield. Approximately 10% of a second product was isolated,

which possessed the C6 bromine but had only two of the secondary hydroxyl groups protected as benzyl ethers. Approximately 20% of the starting material (**122**) was recovered.

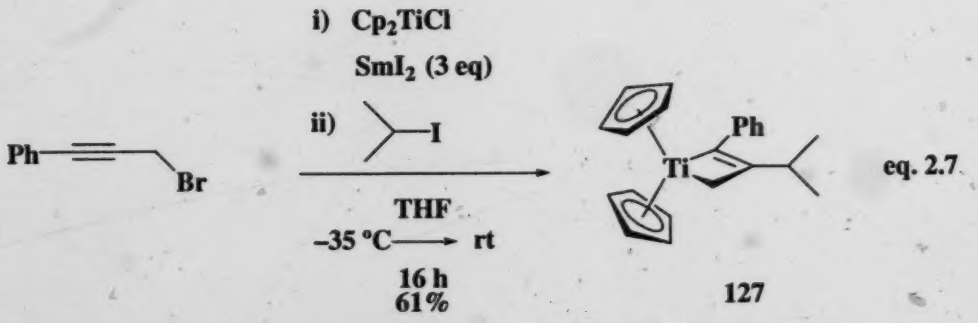
Scheme **2.2**



The product, methyl 2,3,4–tris–O–benzyl–6–bromo–6–deoxy–D–glucopyranoside **126**, exhibits a doublet in the ^{1}H NMR spectrum at δ 4.57 for the hydrogen in the anomeric position (H1) ($^{3}J_{HH}$ = 3.4 Hz). The hydrogens in the ring positions H2, H3, and H4 appear at δ 3.51, 4.01, and 3.53, respectively, as doublets of doublets. The resonances for H5 and H6 overlap in the δ 3.78–3.63 region. The ^{13}C NMR resonances for C1, C2, C3, C4, C5, and C6 appear at δ 98.1, 79.9, 81.9, 77.3, 70.6, and 33.7 consistent with literature values.

ii. Results of titanacyclobutene complex formation

The general procedure for the radical synthesis of titanacyclobutene complexes is exemplified by the following case for the simple compound 1,1–bis(cyclopentadienyl)–3–isopropyl–2–phenyltitanacyclobutene, **127**, (eq. **2.7**). A solution of one equivalent of bis(cyclopentadienyl)titanium(III) chloride and three equivalents of samarium diiodide in



eq. 2.7

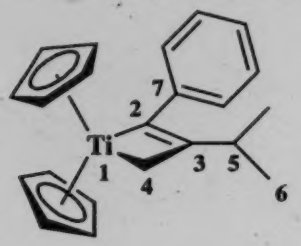
THF were sealed in a medium–walled glass reaction vessel with removable Teflon© stopcock in the glove box. Two more such bombs were prepared, one with a solution of 3–bromo–1–phenylpropyne (one equivalent) in THF, and one containing a known-concentration solution of 2–iodopropane in THF. The glassware is then removed from the box, attached to a Schlenk–line, and the joints evacuated and back–filled with dry nitrogen three times. If air is not judiciously removed, the reaction solution may be exposed to water and oxygen. While titanocenes are compatible with water, an aquo ligand is tenacious and can displace the chloride ligand. The resultant aquo complex is probably inert to the desired chemistry.[62] Oxygen, however, is anathema to titanium(III) and SmI_2 especially, and solutions of these compounds exposed to air discolour rapidly. After the evacuation/backfill cycles, the Teflon stopcocks were replaced with rubber

septa under a moderate nitrogen purge and the Cp_2TiCl/SmI_2 solution was cooled to –35 °C. The 3–bromo–1–phenylpropyne and one equivalent of 2–iodopropane were successively transferred into the vigourously stirred, deep turquoise-blue solution. The colour of the reaction mixture changed to red upon completion of the reaction and a light yellowish-green precipitate of SmX_3 separated. The product **127** was obtained in 61% yield after crystallization from pentane at –35 °C. Selected characterization data of **127** are shown in Table **2.2**.

Carbons 2, 3, and 4 manifest as resonances in the ^{13}C NMR spectrum at δ 210.1, 99.6, and 69.2, respectively. These resonances are diagnostic for titanacyclobutene ring carbons; the chemical shifts are representative of those typically observed for the analogous carbons in other titanacyclobutene compounds.[19,129,131,178,181] The equivalent Cp rings appear in the ^{13}C NMR spectrum at δ 111.4. In the ^{1}H NMR spectrum, the methylene group of the titanacyclobutene ring (H4, H4') appears as a singlet at δ 3.21. This is typical of the chemical shift usually observed from the C4 methylene group. This compound was not characterized by its mass spectrum, however elemental analysis confirms the elemental composition.

In some reactions, it is possible to see the colour of the solution change from turquoise to dark purple before changing to the characteristic red colour of titanocene(IV) compounds. The purple colour may be caused by the mixture of products present at some intermediate stage of reaction that include Cp'_2TiCl_2, which is red, and the titanium(III) species $Cp'_2Ti(\eta^3$–propargyl/allenyl ligand) which is green.[19] In most of the reactions the colour of the solution is red when the reaction is complete, however, in some clean, high

Table 2.2 Characterization data for compound **127**.



127

Atom #	^{13}C NMR resonance (ppm)	^{1}H NMR resonance (ppm)
2	210.1	–
3	99.6	–
4	69.2	3.21 (singlet)
5	27.5	2.67 (septet, $^{3}J_{HH}$ = 5.5 Hz)
6	21.2	0.91 (doublet, $^{3}J_{HH}$ = 5.5 Hz)
7	148.8	–
Cp	111.4	5.58 (singlet)

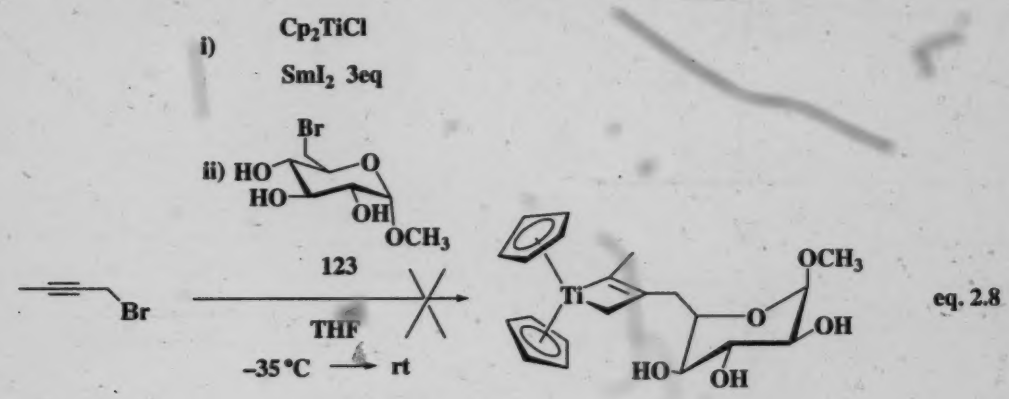
yielding reactions, the solution colour is brown. In all successful reactions, largely insoluble Sm(III) byproducts are formed. The reported titanacyclobutene complexes with cyclopentadienyl, *tert*–butylcyclopentadienyl, and pentamethylcyclopentadienyl ancillary ligands are generally very difficult to purify. Due to their lipophilicity, these complexes are not readily precipitated or crystallized from pentane, hexane, ether, or hexamethyldisiloxane at –35 °C particularly when available in only small (<1 gram

scale). The titanacyclobutene complexes decompose upon contact with neutral alumina or silica gel (judged by the rapid colour change from red to brown). Because of the difficulty in separating the desired compound from the impurities and by–products of the reaction, these by–products were never studied or characterized. If they could be isolated, the nature of these by–products might provide valuable insight into the reaction mechanism.

Naked hydroxyl groups might be anticipated to be deleterious to samarium diiodide–mediated titanacyclobutene complex formation by ligating or chelating the oxophilic titanium or samarium species, altering the dynamics of the reaction.[19] However, it was expected that the fast redox reactions and radical additions would dominate, and allow for formation of titanacyclobutene complex **128** from sugar **123** (eq. **2.8**). In the reaction of bis(cyclopentadienyl)titanium(III) chloride and three equivalents of samarium diiodide with one equivalent of 1–bromo–2–butyne and one equivalent of hexose **123**, this expectation was not met: no identifiable products could be recovered from the reaction mixture.

Protected carbohydrate **126**, however, shows moderate success as a radical source for titanacyclobutene complex construction. The reactions to form titanacyclobutene complexes, however, are not clean and no means has yet been found for the separation of byproducts. Byproducts are in-separable by crystallization using pentane, hexane, diethyl ether, or toluene as solvents. Certain spectroscopic signposts, however, clearly suggest that titanacyclobutene complexes have been formed. For example, in the reaction of

bis(*tert*–butylcyclopentadienyl)titanium(III) chloride, three equivalents of samarium diiodide, one equivalent of 3–bromo–1–phenylpropyne, and one equivalent of methyl

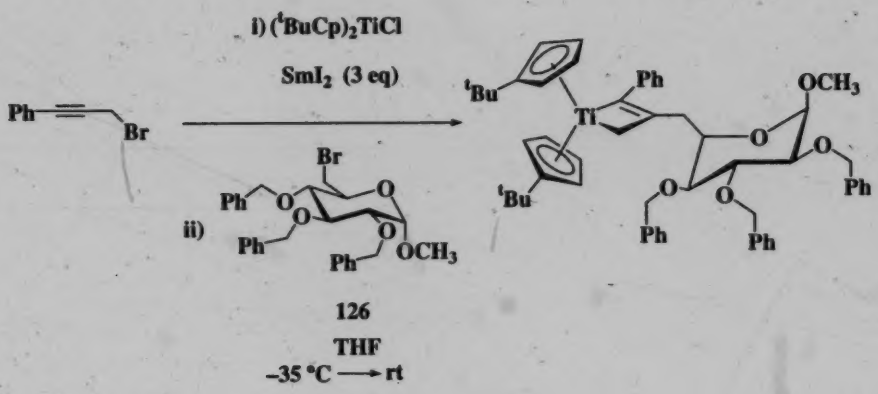


eq. 2.8

128

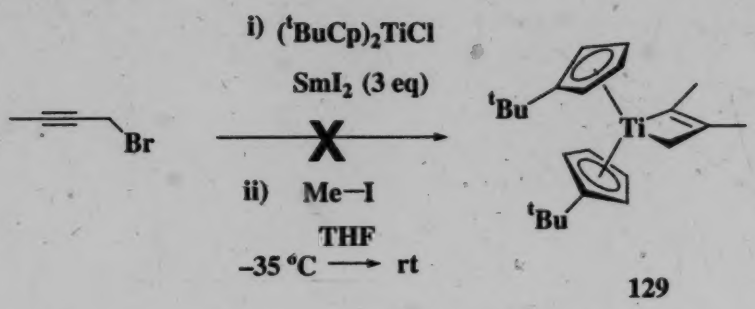
2,3,4–tris–O–benzyl–6–bromo–6–deoxy–D–glucopyranoside **126**, under the general reaction conditions (described above) the colour of the solution turns red and a yellow precipitate forms (eq. **2.9**). The ^{1}H NMR spectrum of the product mixture unfortunately cannot differentiate between unreacted sugar **126**, the titanacyclobutene complex incorporating the sugar residue, and the reduced (*via* H–atom abstraction) sugar. However, the ^{13}C NMR APT spectrum shows resonances at δ 209.1, 100.5, and 72.9, indicative of a titanacyclobutene complex. The presence of the sugar is indicated by the C1 (anomeric) carbon signal at δ 98.2, and C2, C3, C4 ring carbons at δ 75.5, 75.1, and 72.9. Attempts to derivatize then demetallate the titanacyclobutene complex to ascertain its identity by reaction with nitriles (see Chapter Three) were unsuccessful. The use of bis(cyclopentadienyl)titanium(III) chloride also appears to result in titanacyclobutene complex formation, as judged by analogous ^{13}C NMR signals. In the reaction with

bis(pentamethylcyclopentadienyl)titanium(III) chloride, no titanacyclobutene complex formation is indicated.



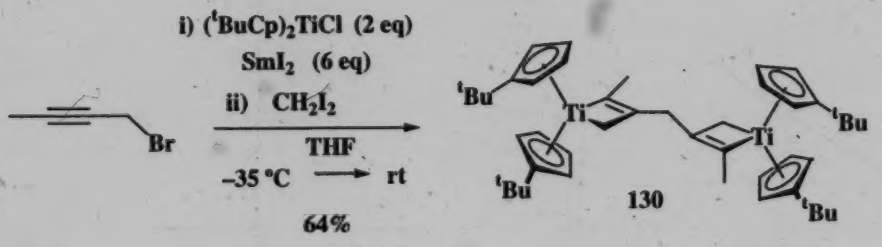
eq. 2.9

Some interesting results were obtained in an attempt to synthesize a series of titanacyclobutene–substituted methane compounds in the *tert*–butylcyclopentadienyl titanocene class. A series of progressively halogenated methanes were used as alkylating radical precursors. The attempted synthesis of the simple titanacyclobutene compound 1,1–bis(*tert*–butylcyclopentadienyl)–2,3–dimethyltitanacyclobutene **129** by the general procedure, using iodomethane as the alkylating radical precursor, resulted in formation of two inseparable products (eq. **2.10**) in an approximate 2:1 ratio. Neither set of signals could be attributed to the expected complex **129**. It might be anticipated that the methyl radical attacks the metal centre. In this scenario, the stabilized propargyl radical would be ejected, leading to the formation of (^{t}BuCp)$_2$Ti(CH$_3$)$_2$. However, this compound is not detected spectroscopically. The major products of this reaction remain unidentified.



eq. 2.10

Both diiodo– and dibromomethane can be used as radical precursors to form a compound in which two titanacyclobutene rings are linked at the central carbons by a methylene bridge. Thus, a THF solution containing two equivalents of 1,1–bis(*tert*–butylcyclopentadienyl)titanium chloride and six equivalents of samarium diiodide was cooled to –35 °C and treated sequentially with two equivalents of 1–bromo–2–butyne and one equivalent of diiodomethane. Linked bis–titanacyclobutene complex **130** is produced in 64% yield (eq. **2.11**). The *tert*–butylcyclopentadienyl hydrogens manifest in the ^{1}H NMR spectrum as broad singlets at δ 5.91, 5.67, 5.51, and 5.42, and the *tert*–butyl



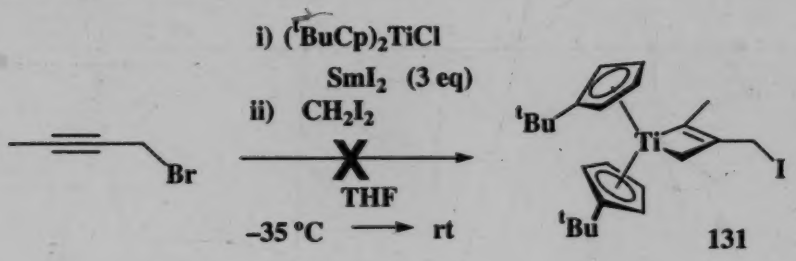
eq. 2.11

group hydrogens as a singlet at δ 1.18. The methylene group of the titanacyclobutene ring appears at δ 3.19, the methyl group on the α–position of the titanacyclobutene ring appears at δ 2.34, and the hydrogens of the methylene bridge appear at δ 2.76. The ^{13}C

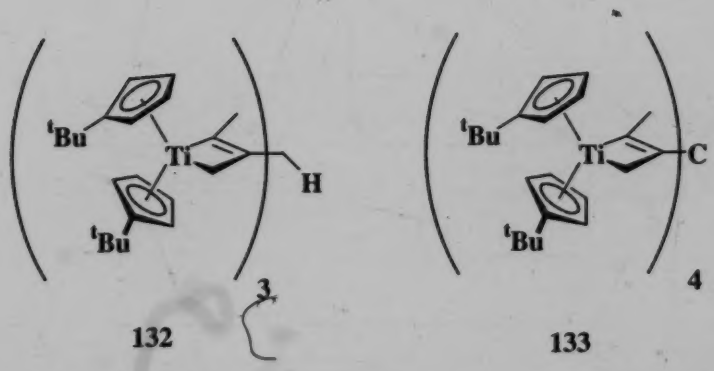
NMR spectrum contains the typical titanacyclobutene ring signals: the α–quaternary carbon appears at δ 211.7, the β–carbon appears at δ 94.9, and the α–methylene carbon appears at δ 76.0. The remaining signals all correspond to the proposed structure. An HMQC experiment was used to reveal the methylene bridge carbon at δ 29.0. Assignments are confirmed by correlated spectroscopy. Complete analysis is given in the Experimental section. A number of attempts to obtain accurate mass data by mass spectrometry failed. Electron impact high resolution mass spectrometry fails to provide a parent *m/z* peak, as does electrospray ionization mass spectrometry (positive ionization). Chemical ionization using ammonia gas (positive ionization) also failed to yield a parent *m/z* peak, showing instead a 705.2 peak, corresponding to the parent molecule with incorporation of five hydrogens, as well as a 721.2 peak which corresponds to the parent molecule with incorporation of 4 hydrogens and one ammonia molecule. Use of dibromomethane as the alkylating radical also provides linked complex **130** cleanly, in 62% yield.

Titanacyclobutene complexes with functional groups would be useful for subsequent functionalization, and so the synthesis of the titanacyclobutene complex bearing a pendant iodomethyl group **131** was attempted (eq. **2.12**). A cold THF solution of one equivalent of 1,1–bis(*tert*–butylcyclopentadienyl)titanium chloride and three equivalents of SmI_2 was treated sequentially with 1–bromo–2–butyne and one equivalent of diiodomethane. However, under the standard reaction conditions employed, no iodomethyl compound **131** was produced, and only an unquantified amount of the bridged compound **129** was cleanly formed. The syntheses of the tri–substituted (**132**)

and tetra–substituted (**133**) methane derivatives were attempted using bromoform and carbon tetrabromide as the alkylating radical precursors, however only unidentifiable products were returned.



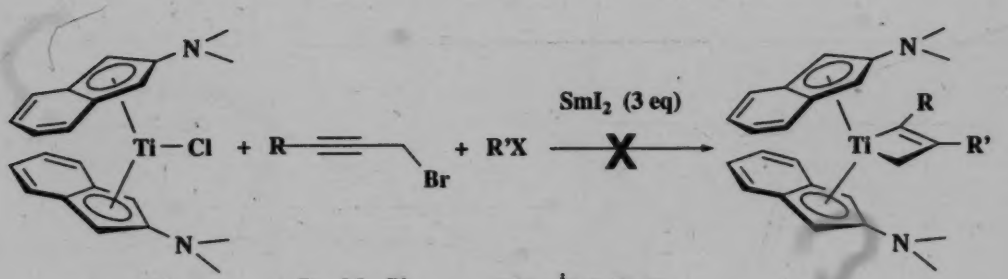
eq. 2.12



Due to the differences in reactivity between compounds bearing the pentamethylcyclopentadienyl, *tert*–butylcyclopentadienyl, and cyclopentadienyl ancillary ligand sets towards radical alkylation reactions, the effect of a fourth Cp–template was briefly studied. Bis(N,N'–dimethylaminoindenyl)titanium (III) chloride **134** $(DMAI)_2TiCl$ was chosen under the thesis that a more electron–rich titanium species would better facilitate the alkylation reactions and perhaps offer cleaner products in shorter time.[27] $(DMAI)_2TiCl$ was employed in a variety of reactions known to yield titanacyclobutene product with other Cp templates, but did not offer the same results.

Not even trace amounts of titanacyclobutene products were detected. Some attempted reactions are shown in Scheme **2.3**.

Scheme **2.3**

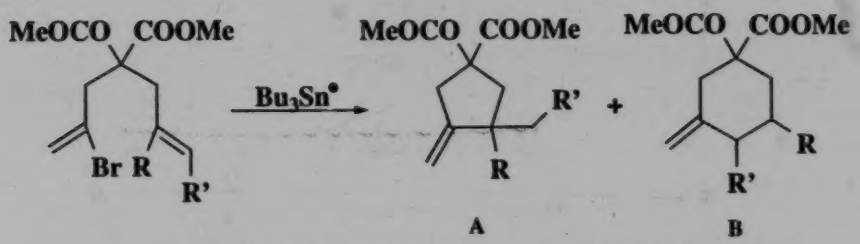


134 **R = Me, Ph** **R'X = ^{i}PrI, BnCl**

B. Intermolecular Vinyl Radical Addition Reactions.

The utilization of radical methodologies in the context of organic synthesis is a well established field.[137] Within that domain, the creation and exploitation of vinyl radicals is synthetically valuable.[4b,c] A common method of generating vinyl radicals is by stannane abstraction of a vinyl halide, as illustrated in Scheme **2.4**. This example also demonstrates the influence of alkyl substituents on the radical acceptor moiety on the relative ratio of five–exo–trig *versus* six–endo–trig cyclization products.[4b] Radical attack at the less hindered position is favoured both sterically and by the stabilizing influence of the alkyl substituent on the newly–formed radical centre. Another method of vinyl radical creation is by addition of a tin radical to a triple bond. Subsequent intramolecular cyclization to form an *exo*–cyclopentene is shown in Scheme **2.5**.[138]

Scheme 2.4

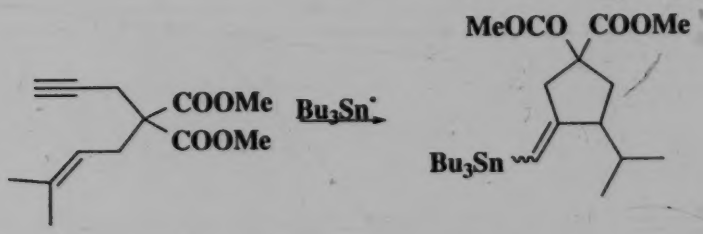


Stork, G.; Baine, N.H. *J. Am. Chem. Soc.* **1982**, *104*, 2321.

R	R'	Ratio A:B
H	H	3:1
CH_3	H	only B
H	CH_3	2:1

Vinyl radicals are much more difficult to create directly than alkyl radicals, with C–X bond dissociation constants about 5 kcal/mol greater,[139,140,141,142,143] and are much more reactive, making troublesome and unproductive competing reactions, such as H

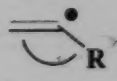
Scheme 2.5



Stork, G.; Mook, R. Jr. *J. Am. Chem. Soc.* **1987**, *109*, 2829.

atom extraction from donor solvents, a potential concern. Like alkyl radicals, vinyl radicals invert rapidly. The configurations of vinyl radicals can be either linear or bent, depending largely on the α–substituent.[144] Vinyl radicals **135** with σ–type α–substituents (Me, OH, Cl) are bent, with an inversion barrier that increases as the electronegativity of the substituent increases (Figure **2.1**). For vinyl radicals with an α–methyl group, a bent structure with a bond angle of 141° is found to be the minimum energy structure. The inversion barrier is calculated to be very low: 3.1 kcal/mol. The rapid epimerization of vinyl radicals precludes the retention of stereochemistry in the product. Pioneering work with vinyl radicals demonstrated that the *cis*– and *trans*–peresters **136** and **137** independently undergo thermal decomposition in cumene to afford the same ratio of *cis*– and *trans*–2–phenyl–2–butenes, **138**, **139**, *cis/trans* = 1.1–1.2 (Scheme **2.6**). The rapidly equilibrating vinyl radicals generated react predominantly by H–atom abstraction from the cumene solvent; dicumyl is isolated as one of the byproducts of the reaction.[145]

Figure 2.1

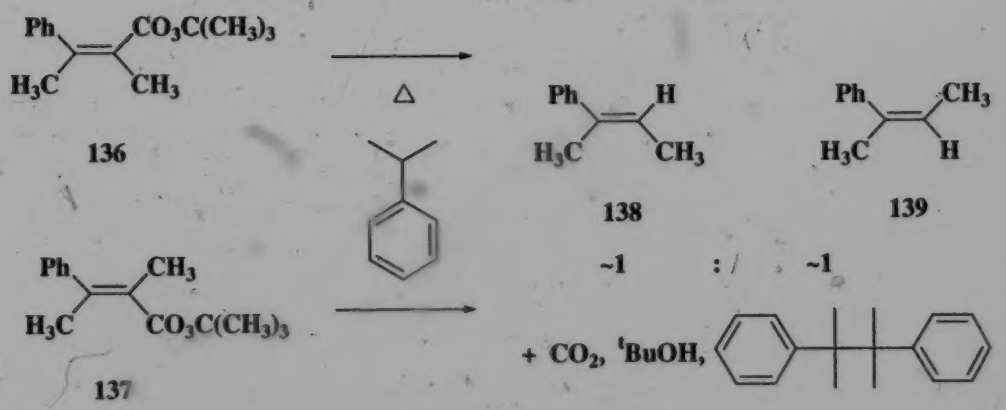


135

R	Bond angle (deg)	Inversion barrier (kcal/mol)
H	138	3.3
CH_3	141	3.1
Cl	134	11.1
F	129	19.5

The ability to use radical sources other than alkyl and propargyl halides to alkylate *in situ* derived η^3–propargyl titanocene complexes would be a substantial step forward in expanding the synthetic utility of this process. The addition of vinyl radical methodology to the repertoire of synthetic methods available to construct titanacyclobutene compounds *via* radical alkylation of propargyl complexes makes it possible to construct a new class of titanacyclobutene complexes and expand the scope of synthetic possibilities for these organometallic molecules. Vinyl radicals provide a way to create carbon–carbon bonds between sp^2 carbons in the titanacyclobutene complex product. In addition, alkylation of an η^3–propargyl titanocene complex with a vinyl radical affords a conjugated diene, a useful organic synthon.

Scheme **2.6**



Due to the strength of the carbon–bromine bond in the vinyl halide radical precursors, however, direct reduction to form vinyl radicals from alkenyl bromides *via* either samarium diiodide or titanocene(III) chlorides is not possible. A stronger yet

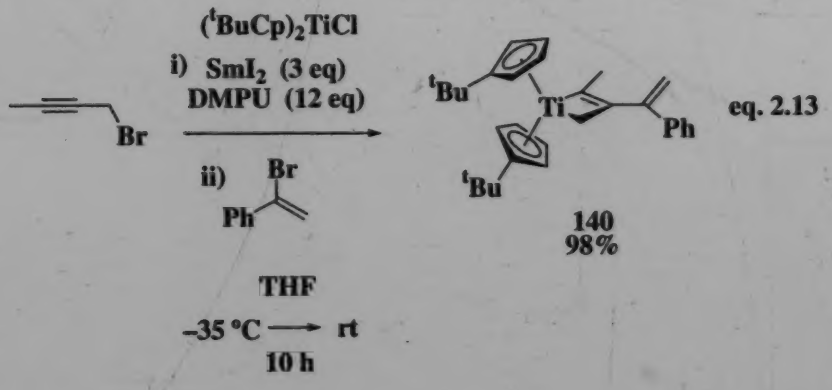
selective reductant is required: one sufficiently powerful to induce carbon–bromine bond homolysis, but mild enough to be compatible with the titanium(III) and titanium(IV) complexes present in the reaction.

While vinyl radicals can not be generated by samarium diiodide alone, with the appropriate choice of additive, the oxidation potential can be made negative enough to affect halogen atom abstraction by the samarium reductant species. The reductant formed by the addition of HMPA or DMPU to solutions of SmI_2 is powerful enough to reduce vinyl bromides to vinyl radicals (page 49). Problems with the yields and universality of this procedure exist, primarily due to the high reactivity of the vinyl radical, which can abstract H–atom from the surrounding THF solvent to yield the corresponding reduced alkene.

Results

The general procedure used to synthesize these compounds is similar to that discussed earlier for alkyl and benzyl radical-derived titanacyclobutene complexes, the difference being in the addition of the SmI_2-complexing reagent (HMPA or DMPU). The procedure is briefly discussed for the synthesis of 1,1-bis(*tert*-butylcyclopentadienyl)-3-(1-phenylethene)-2-methyl-titanacyclobutene **140** (eq. **2.13**). Bis(*tert*–butylcyclopentadienyl)titanium chloride and three equivalents of samarium diiodide in THF were cooled to –35 °C. 1–Bromo–2–butyne was added and the solution was kept at –35 °C for two minutes. In this time the colour of the solution changed from turquoise to brown; this was taken to indicate the consumption of the 1–bromo–2–butyne by formation of

either or both of titanium(IV) complex **141** and titanium(III) complex **142**. Cold (–35 °C) DMPU (12 equivalents), was then added to the solution. After the addition of DMPU, the solution was no longer homogeneous: a purple and white precipitate was formed, presumably as a result of the lower solubility of the SmI_2(DMPU) complex in THF.[146] The vinyl halide, α–bromostyrene, was then added and the solution was maintained at –35 °C for ten minutes before warming to room temperature. The solution was stirred at room temperature for 16 hours at which point the colour becomes red. After evaporation of the solvent, the residue was triturated with pentane and then filtered through a Celite plug on a cinter. Evaporation of the solvent afforded clean product. The



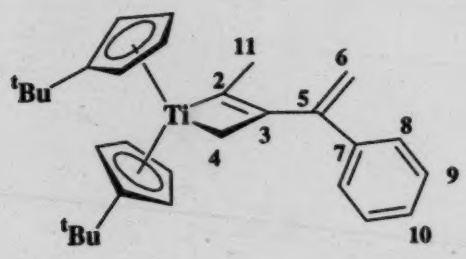
141 **142**

titanacyclobutene complex **140** was also synthesized by the same procedure but employing twelve equivalents of HMPA rather than DMPU to form the samarium reductant. There is no observable difference in the reactions run with these two

additives: HMPA also forms a purple complex with SmI_2 in THF, and the resulting complex is not homogenous at the concentration employed. The titanacyclobutene complex is spectroscopically identical to that formed by the SmI_2(DMPU) reductant. Care must be taken to add exactly, or slightly less than, four equivalents of HMPA per equivalent of samarium diiodide. Reactions to form titanacyclobutene complexes are typically worked up by evaporation of the THF solvent under reduced pressure, followed by trituration of the residue with pentane. The relatively non–polar titanacyclobutene complexes dissolve in the pentane, whereas the Sm(III) byproducts are quite insoluble and easily separated by filtering the pentane through Celite. Up to four equivalents of HMPA stay bound to the SmX_3 complex,[83,93] and are thus separated from the target material. However if an amount greater than four equivalents is used, the excess is extracted with the target material.

Structural assignment for **140** follows from a comprehensive analysis of the spectroscopic data, summarized in Table **2.3**. The ^{1}H NMR data of **140** gives characteristic signals for the presence of a bis(*tert*–butylcyclopentadiene)titanacyclobutene complex. The *tert*–butylcyclopentadienyl ligands set gives rise to four quartets at δ 5.91, 5.63, 5.58, and 5.44 with coupling constants of 2.3 Hz. The two vinyl hydrogens on complex **139** (H6 and H6') appear at δ 5.42 and δ 4.91 as doublets with ^2J = 2.0 Hz. The ^{13}C (APT) NMR spectral data are also consistent with the presence of a titanacyclobutene moiety. The α and β quaternary carbons, as well as the α–methylene ring carbons in compound **140** come at δ 212.3 (C2), 99.3 (C3), 72.9 (C4) respectively.

Table **2.3** Selected characterization data for compound **140**.

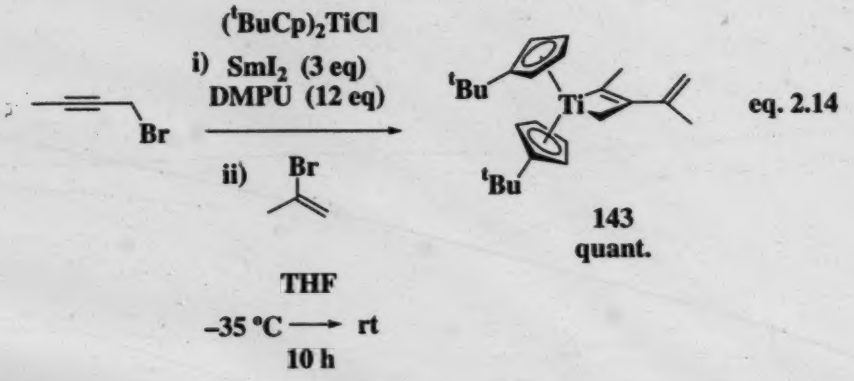


140

Assignment	^{1}H NMR (300 MHz, C_6D_6) (ppm)	^{13}C NMR (75 MHz, C_6D_6) (ppm)
2	–	212.3
3	–	99.3
4	3.22 (q, J = 2.0 Hz)	72.9
5	–	72.9
6	5.42 (d, J = 2.0 Hz) 4.91 (d, J = 2.0 Hz)	111.9

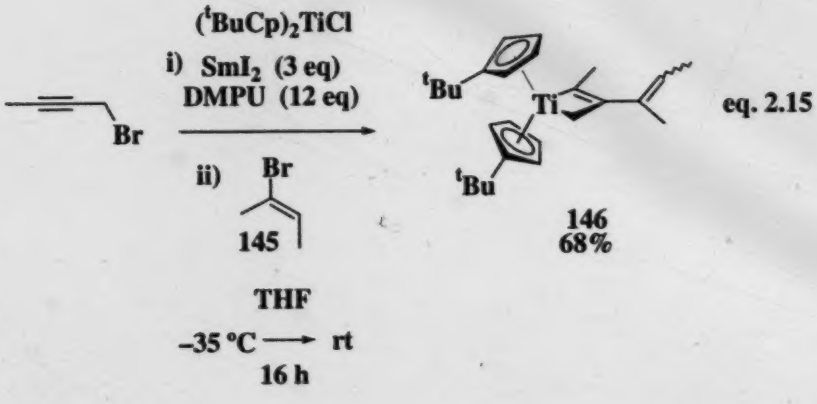
1,1–Bis(*tert*–butylcyclopentadienyl)–3–isopropenyl–2–methyltitanacyclobutene **143** was synthesized by the same general procedure using both DMPU and HMPA as the additives to form the samarium reductant (eq. **2.14**). A comparison of selected data between the two vinyl radical addition products, **140** and **143**, and a typical alkyl radical addition product, **144**, is shown in Table **2.4**. Because the numbering schemes for each of the complexes provides different labels for analogous carbons, the positions of interest

are labelled alphabetically, for consistency. By ^{13}C NMR chemical shifts, the effect of the extra conjugation on the carbons that comprise the titanacyclobutene ring is minimal. Visually, dry, solid samples of the vinyl radical adducts **140** and **143** are deep red in colour; very similar to benzyl radical adduct **144** and other *tert*–butylcyclopentadienyl titanocene–derived titanacyclobutene complexes.



eq. 2.14

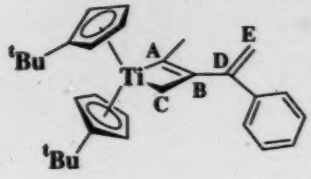
Vinyl halide *trans*–2–bromo–2–butene **145** reacts to give titanacyclobutene products **146**, but returned an inseparable mixture of alkene isomers (equation **2.15**). Due



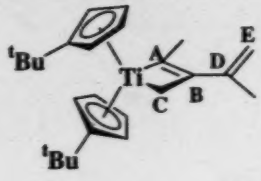
eq. 2.15

to the rapid inversion of vinyl radicals[144] retention of the stereochemistry of the double bond is not seen. The ^{1}H NMR spectrum is not very useful for interpreting the products of this reaction but suggests an approximate 2:1 ratio of the two isomers. However, the ^{13}C NMR spectrum clearly suggests the presence of two titanacyclobutene complexes by the doubling of resonances at δ 211.1, 210.2, 100.7, 97.5, 73.5, and 72.1. By analogy to compounds **140** and **143** (Table **2.6**), quatenary alkene carbons appear at δ 139.5 and 139.4 for the putative two titanacyclobutene isomers. The mass is confirmed by HRMS.

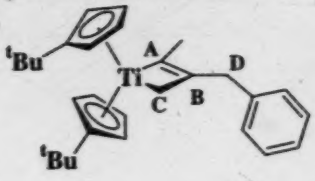
Table **2.4** Comparison of selected spectral data for compounds 140, 143, 144



140



143

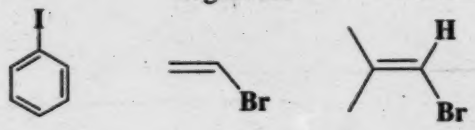


144

Selected data NMR chemical shifts	1,1–Bis(*tert*–butylcyclopentadienyl)–3–(1–phenylethene)–2–methyltitanacyclobutene **140**	1,1–Bis(*tert*–butylcyclopentadienyl)–3–(isopropenyl)–2–methyltitanacyclobutene **143**	1,1–Bis(*tert*–butylcyclopentadienyl)–3–(benzyl)–2–methyltitanacyclobutene **144**
(^{1}H) vinyl hydrogens	δ 5.42, 4.91	δ 5.06, 4.72	
(^{13}C) carbon A	δ 212.3	δ 211.1	δ 207.8
(^{13}C) carbon B	δ 99.3	δ 99.7	δ 95.9
(^{13}C) carbon C	δ 72.9	δ 70.6	δ 72.3
(^{13}C) carbon D	δ 147.9	δ 142.9	δ 35.5
(^{13}C) carbon E	δ 111.9	δ 111.6	

Additionally, other vinyl halides were investigated as sources of vinyl radicals in an effort to demonstrate generality. Iodobenzene failed to yield tractable products, as did either vinyl bromide, or 1–bromo–2–methyl–propene **147** (Figure 2.2).

Figure 2.2



147

The criteria that discriminate between the vinyl halides that undergo successful reactions to form titanacyclobutene complexes and those that do not proceed are unclear from these preliminary findings.

Additives other than DMPU and HMPA were also investigated as potential partners for the SmI_2/ligand reduction complex. Visible light,[118] LiCl,[116] LiBr,[116] and H_2O[113] are all reported to increase the oxidation potential of SmI_2.[109] All of the above, however, failed to afford clean product in the above reactions under the typical reaction procedure.

C. Medium and Large Ring Synthesis *via* Intramolecular Alkyl Radical Cyclizations of Titanium (III) Propargyl Complexes.

The construction of cyclic organic compounds is an important aspect of organic chemistry.[147] Of the many methods for constructing such compounds, such as

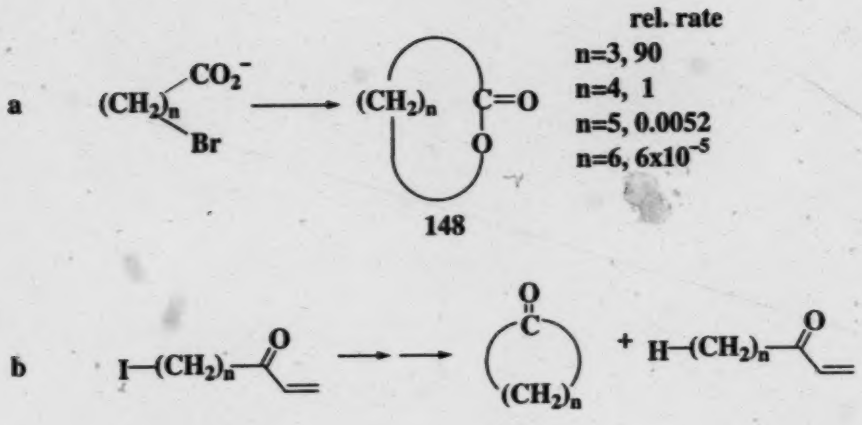
cycloaddition reactions and ring–closing metathesis reactions,[148] the most common are cyclization reactions. However, not every ring size can be synthesized by a cyclization reaction with the same facility. Typically five– and six–membered rings are easily constructed, but a precipitous decline in yields occurs with smaller and larger ring sizes. A large number of examples have served to establish a rough correlation between the rate of cyclization (k_C) and the size of the ring formed.[149] For example, the rate of formation of lactones **148** by carboxylate displacement of a ω–bromide exhibits a range of five orders of magnitude between the five– and eight–membered rings (**Scheme 2.7a**).[150] Enthalpic and entropic considerations are responsible for the large differences in ease of formation. The $\Delta H^{\ddagger}$ for formation of three– and four–membered rings is typically greater than the $\Delta H^{\ddagger}$ for formation of five– and six–membered rings. The $\Delta H^{\ddagger}$ term reflects the strain which develops in the transition state for ring closure; ring strain for cyclopropane and cyclobutane is approximately 27 kcal/mol, whereas ring strain is much less for cyclopentane (6.3 kcal/mol) and cyclohexane (~1 kcal/mol). [151] The entropy term, $\Delta S^{\ddagger}$, is the least negative for three–membered ring formation, comparable for four–, five–, and six–membered ring formation, and becomes more negative as the ring size increases past seven. The larger entropy associated with eight–membered and greater ring size reflects the relative improbability of achieving the required transition state orientation. Because the combination of enthalpic and entropic factors is the most favourable for five– and six–membered rings formation, the maximum rate of formation is observed for these sizes. An effort to correlate the ease of ring closure with stereoelectronic requirements was forwarded by Baldwin.[152] Cyclizations are classified according to three criteria: (a)

ring size, (b) hybridization of the reactive site carbon, and (c) endo– or exocyclic ring closure. The overriding aspect governing cyclization is ease of approach of the nucleophile to the LUMO of the leaving group bond.

The construction of cyclic compounds by radical methodology offers an alternative to ionic methods.[153] Carbon radical cyclization onto a 5,6 carbon–carbon double bond (structure **91**, Scheme **1.23**, page 55) can result in the formation of either five– or six–membered ring compounds, or both. The five–membered ring formation is prefered kinetically, even though 5–exo closure results in the formation of a less stabilized primary radical, while 6–endo closure results in a secondary radical. Although formation of the five–membered ring is generally faster, six–membered ring formation is favoured thermodynamically. For example, in the case of a 5–hexenyl radical in which the original radical centre is non–stabilized, and in the presence of good hydrogen donors, the reaction is under kinetic control. In these reactions H–atom abstraction traps the rapidly formed radical, yielding largely the five–membered ring compound ($k_C = 1.0 \cdot 10^5\ s^{-1}$, $E_a = 6.1$ kcal/mol).[154] However, if the original radical centre is stabilized and there are no good hydrogen donors present, cyclization to form the five–membered ring is reversible. The overall reaction is then thermodynamically controlled, and favours the six–membered ring.[155] As with the ionic cyclization reactions discussed above, intramolecular radical cyclizations are governed in part by entropic considerations, although other factors[156] such as the presence of substituents on the double bond, may be relevant.[4b,c]

The intramolecular addition of a radical onto a proximal carbon–carbon double bond to form a five– or six–membered ring occurs easily but until recently larger ring sizes were not available in a synthetically useful sense by radical cyclization reactions. As such, there are few methods available to construct medium and large ring carbocycles using radical methodology. Porter has demonstrated that free radical cyclization to form macrocyclic ketones [157] and lactones is feasible.[158] Sequential radical cyclizations have been used to construct macrocyclic transannular compounds.[159] For example, the series of acyclic enones **149–151** were studied as substrates for intramolecular radical cyclization (Scheme **2.7b**). Intramolecular *endo* cyclization of compound **149** to form the ten–membered ketone **152** proceeds in the lowest yield of the three, providing only 15% of the cyclization product, and 27% of the reduced, acyclic product **153**. In contrast, the cyclization reaction of enone **150** proceeds to form 14–membered ring ketone **154** in 63% yield. The acyclic product **155** is formed in 22% yield. The optimized conditions for the macrocyclization reactions were determined.[157] The optimum concentration for the alkyl iodide enone substrate was determined to be in the 3–6 mM range: the alkyl iodide, 1.1 equivalents of tributyltin hydride and 0.1 equivalents of AIBN are refluxed in dry benzene. Reactions carried out at higher concentrations of substrate and tin hydride give more acyclic product and generally lower overall product yield than those carried out at 3–6 mM. This increase in acyclic product results from increased H–atom transfer to the acyclic radical. Lower overall product recovery may result from competitive intermolecular radical coupling. The rate constant for the formation of the 14–membered ketone **154** was determined to be $k_C = 1.2 \times 10^4\ s^{-1}$.[157]

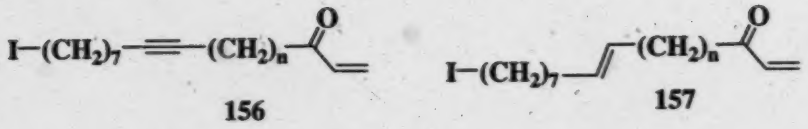
Scheme 2.7



acyclic enone	n	cyclic product (% yield)	acyclic product (% yield)
149	7	**152** (15)	**153** (27)
150	11	**154** (63)	**155** (22)
151	15	(54)	(16)

The corresponding 12–membered ring unsaturated ketones were formed with the unsaturated acyclic substrates **156** and **157** (Figure **2.3**). Interestingly, the yields for the cyclization products are much higher than for the saturated substrates, and the amount of acyclic product is much less. The triple–bond containing substrate **156** undergoes cyclization to form the 12–membered ketone in 76% yield, with only 6% of the acyclic reduced product formed. Double–bond containing substrate **157** produces 78% of the cyclic ketone, and only 8% of the reduced acyclic product. Transannular cyclization of these substrates is not detected.

Figure 2.3

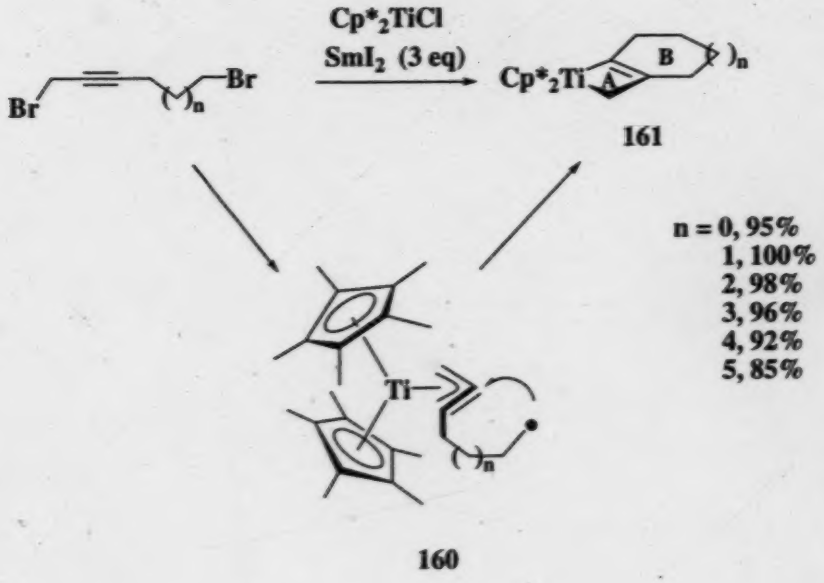


156 157

Within the domain of organometallic chemistry the inherent qualities of certain metal–ligand combinations can be exploited to facilitate large ring synthesis. Attack of a carbon–based radical on a metal–bound ligand can be influenced electronically and physically by other ligands on the metal. The Stryker group has previously used the templating effect of ancillary pentamethylcyclopentadienyl ligands to synthesize medium and large carbocycles by intramolecular radical cyclization onto bound η^3–propargyl/allenyl moieties.[28] The acyclic long chain substrates employed for the syntheses contain a propargyl bromide terminus, which eventually becomes the η^3–propargyl/allenyl ligand, and a primary alkyl bromide terminus, which becomes the alkylating agent (Scheme **2.8**). There are two important aspects of these cyclization reactions. The first is that in a single step—radical "attack" by the free terminus of the tether onto the bound central carbon of the propargyl moiety (**160**, Scheme **2.8**)— the acyclic substrate becomes bicyclic structure **161**, incorporating titanium and two pro–chiral carbon centres. The structure is similar to those discussed in the previous section; containing a titanacyclobutene core (A–ring), onto which is appended a second ring (B–ring) through carbons 2 and 3 of the titanacyclobutene ring. Secondly, by virtue of the influence of the titanocene portion of the molecule, a radical cyclization is facilitated that

would not occur in its absence. The physical space occupied by the Cp ligands restricts the range of motion available to the potential alkylating radical terminus of the tether, as well as providing Thorpe–Ingold[160] type[161] entropic assistance. These factors, in combination with the fixed orientation of the bound propargyl/allenyl moiety, results in a "templating" ability that may facilitate the radical alkylation reaction despite the large ring size. In the pentamethylcyclopentadienyl series, B–ring sizes of five, six, seven, eight, nine, and ten have been constructed in high yields without resorting to high dilution techniques.[28]

Scheme **2.8**

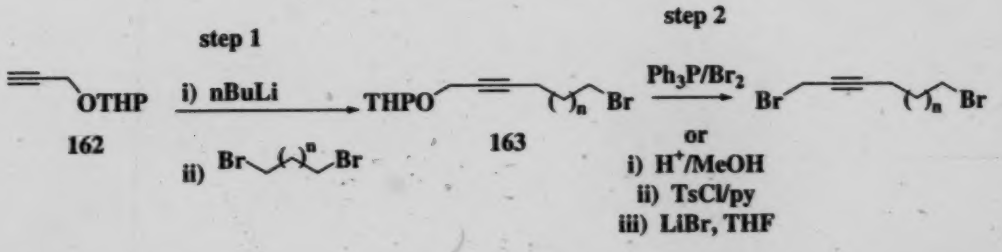


i. Substrate synthesis

To probe the maximum ring size that can be constructed using this technology, substrates were constructed which, if successful, would yield titanacyclobutene complexes with appended 10, 12, and 14–membered rings. These α,ω–dihalo–2–yne substrates were synthesized in a straightforward manner.[162] The lithium salt of 2–propynyloxy–tetrahydropyran **162** was generated by n–BuLi mediated deprotonation in liquid ammonia at –50 °C, and alkylated with one equivalent of the appropriate α,ω–dibromo alkane to afford the THP ether intermediates, **163** (Table **2.5**).[163] The ammonia was dried immediately prior to use by distillation over sodium metal, then re–condensed into the reaction vessel. Even with dry ammonia,[164] however, the mono–alkylation steps were very low yielding and extending the reaction time did not result in any substantial gain in yields. Protected propargyl alcohol intermediates **163** were converted to the desired α,ω–dibromo–2–ynes by one of two methods. The unquantified crude material was usually carried forward to the final product without isolation or purification. Direct reaction using PPh_3/Br_2[165] provides high yields of the desired bromide. This procedure is indicated by "step 2" in Table **2.7** for compounds **165** and **166**. The target material is readily separated from the reaction by–products by silica gel chromatography. The propargyl substrate 1,13–dibromopropadeca–2–yne **165** was obtained by this method from the THP–protected alcohol cleanly in 81% yield. 1,15–dibromopentadeca–2–yne **166** was obtained in 99% yield. By this method, compound **164** was inseparable from one of the by–products of this reaction, however, and had to be synthesized by another route. In this case, the corresponding THP ether **163** was deprotected by the action of a

catalytic amount of PPTs in MeOH/THF at reflux to yield the crude propargyl alcohol which was carried on to the next step directly.[166] The unprotected propargyl alcohol was converted to the methyl sulfonate ester by reaction with methanesulfonyl chloride and triethyl amine, and the crude product carried onto the next step directly. The final product **164** was obtained by displacement of the sulfonate group with lithium bromide to yield the desired dibromide as an analytically pure sample after workup. The overall yield of the transformation of the THP ether **163** to 1,11–dibromoundeca–2–yne **164** by this three–step method is 61%. This procedure is indicated by "step 2" in Table **2.5** for compound **164**.

Table **2.5** Synthesis of α,ω–dibromo–2–ynes



α,ω–dibromo–2–yne	n	Step 1 Time (h)	Step 1 Yield (%)	Step 2 Yield (%)
164	6	16	26	61‡
165	8	20	27	81
166	10	120	15	99

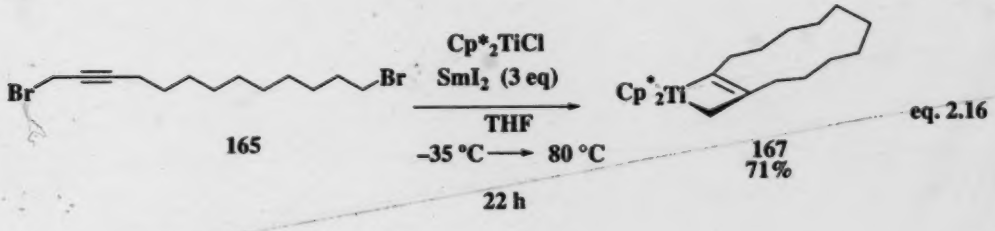
‡: yield given is product of three steps (91%, 98%, 69%) (see text for explanation)

ii. Results

The most important observation in this chemistry is that the maximum size of the B–ring that can be formed is dependent on the identity of the ancillary ligand set. For the pentamethylcyclopentadienyl series, a B–ring size as large as 12 could be obtained in synthetically acceptable yield.

The bicyclic compounds were synthesized according to the general method discussed previously. Heating the reaction mixture to approximately 80 °C was sometimes necessary to effect the cyclization in a reasonable time period. For example, the attempted cyclization reaction of 1,13–propadec–2–yne left at room temperature for several days showed little or no conversion to the product. However, heating the solution briefly allows for good yield of the desired product. Thus, a solution of bis(pentamethyl-cyclopentadienyl)titanium(III) chloride and samarium diiodide (three equivalents) treated with 1,13–propadec–2–yne **165**, upon heating to 80 °C for six hours, resulted in the formation of 13,13–bis(pentamethylcyclopentadienyl)titanabicyclo[10.2.0]–butadeca–1–(12)–ene **167** in 71% yield as a brown–red oil (eq. **2.16**). The ^{1}H NMR spectrum is not very useful in ascertaining purity or identity. Many of the hydrogen signals are centred approximately at δ 1.47, and are therefore somewhat obscured by the pentamethylcyclopentadienyl methyl groups. The ^{13}C NMR spectrum however is diagnostic for titanacyclobutene formation: signals appear at δ 212.1, 105.5, and 78.4. The quaternary carbons of the pentamethylcyclopentadienyl ligands appear at δ 117.8, and the carbon of the methyl groups appears at δ 12.1. The carbons of the B–ring are

indistinguishable between δ 31.6 and δ 29.5. Variable temperature NMR experiments in toluene-d_8 between –90 °C and 60 °C failed to separate out the signals. Attempts to construct the titanabicyclobutene complex with a 14–membered B–ring failed despite a variety of modifications to the procedure, including varying the temperature of the titanium(III)/samarium(II) solution to which the propargyl substrate is added, and varying the reaction times and temperatures. The concentration of the solution was not varied, however. Intermolecular processes may become important at this chain size, and high dilution techniques may be required, however head-to-tail intermolecular dimerization products were not detected by HRMS.



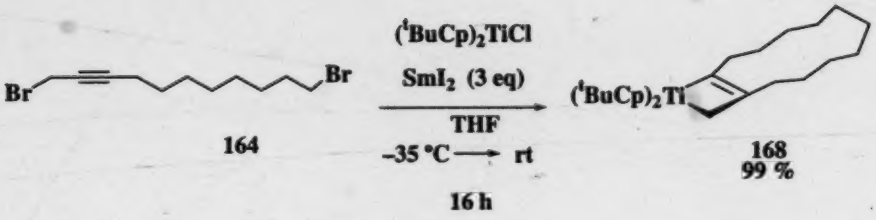
eq. 2.16

The reaction of one equivalent of bis(*tert*–butylcyclopentadienyl)titanium(III) chloride and three equivalents of samarium diiodide with 1,13–propadec–2–yne **165** by the same procedure in order to synthesize the corresponding twelve-membered ring titanacyclobutene complex yields a mixture which likely contains more than one compound, one of which is probably a titanacyclobutene complex. The titanacylobutene ring is indicated in the ^{13}C NMR spectrum by a single low–field resonance at δ 220, as well as a signals at δ 106 and δ 71. However, a surfeit of signals, especially in the δ 42–

occur, and that under high dilution conditions the desired product could be synthesized more cleanly.[157] This compound, like other titanacyclobutene complexes with cyclopentadienyl, *tert*–butylcyclopentadienyl, and pentamethylcyclopentadienyl ligands, is difficult to purify. Attempted crystallizations of ~ 250 mg of the crude mixture from pentane, hexane, and ether at –35 °C each failed. Purification was attempted by size exclusion gel chromatography as size exclusion gel[167] does not react to an appreciable extent with the titanium complex. Unfortunately, this technique did not separate the product from the impurities.

In the *tert*–butylcyclopentadienyl ancillary ligand set, a maximum B–ring size of ten has been observed under the standard reaction conditions. 11,11–Bis(*tert*–butylcyclopentadienyl)titanabicyclo[8.2.0]–dodeca–1–(10)–ene, **168**, is formed quantitatively by the cyclization of 1,11–undeca–2–yne **164** in 99% yield at room temperature (eq. **2.17**). The ^{1}H NMR spectrum exhibits two broad low–field signals at δ 6.03 and δ 5.49, in a ~ 1:4 ratio. These are presumably the ring hydrogens of the *tert*–butylcyclopentadienyl ligands, but because of the errant ratio, another compound may be present. The presence of a major impurity is not indicated by the ^{13}C NMR spectrum, however. Sixteen resonance signals are visible, including titanacyclobutene ring resonances at δ 216.7, 95.2, and 75.2. Four signals are manifest in the region particular for the tertiary ring carbons of the *tert*–butylcyclopentadienyl ligands, δ 110.5, 109.9, 108.9, and 106.2, and one in the region particular for the quarternary ring carbon, at δ 138.7. The quarternary carbon of the *tert*–butyl group is visible at δ 37.6, and the carbon of the methyl group is visible at δ 31.6. Eight other resonances appear at δ 32.2, 30.8,

30.4, 30.2, 29.9, 29.7, 29.4, and 28.2. No extra signals that would indicate an impurity are visible in the ^{13}C NMR spectrum.

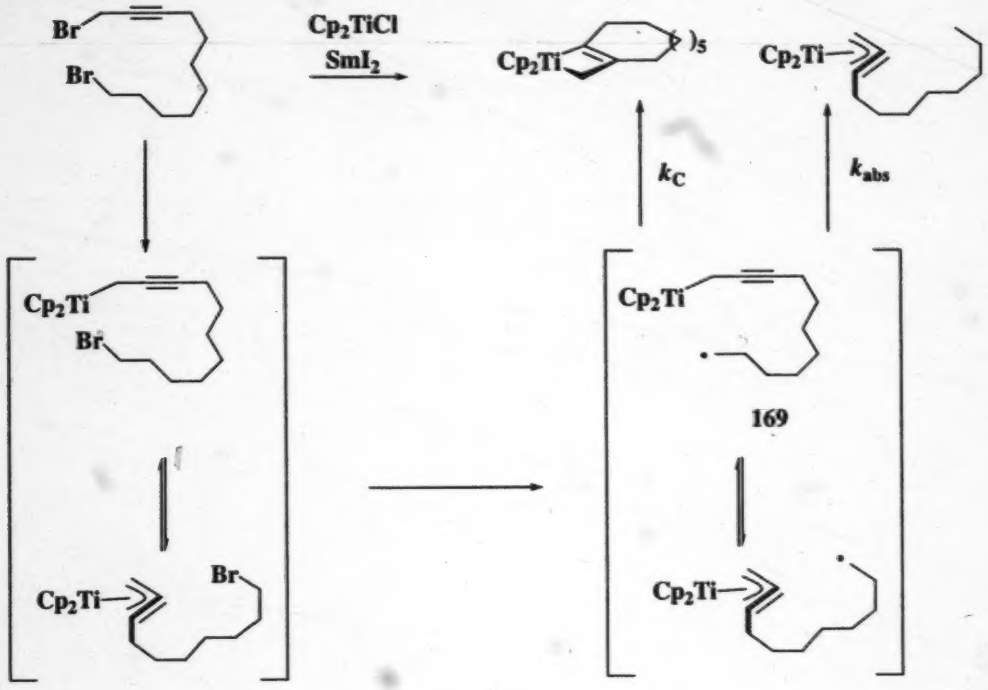


eq. 2.17

In the Cp series, not even the ten–membered ring could be formed under the general reaction conditions. It was reasoned that the lack of desired reactivity may be due to a reduced templating effect as a result of the smaller steric profile of the cyclopentadienyl ligand compared to the *tert*–butylcyclopentadienyl ligand, and partially due to the manner in which the primary alkyl halide terminus of the substrate was reduced. The reduction of an alkyl halide or alkyl halide moiety in the titanacyclobutene complex forming reactions is thought to occur by halide abstraction by some titanium(III) species. The samarium diiodide serves to reduce the titanium(IV) (alkyl)(halide) complex. With substrates designed for intramolecular cyclization, there exists the possibility that intermolecular processes can occur. In this scenario, the titanium(III) propargyl species, formed in the usual manner, loses bromine atom to form the putative radical intermediates **169**. If the templating effect of the ligand set is insufficient to facilitate the cyclization reaction, or the cyclization reaction is relatively slow, these intermediates may undergo competitive intermolecular processes, and hydrogen atom abstraction to form the reduced compound may become the dominant reaction (k_{abs} >>

k_C) (Scheme 2.9). In an effort to alter the dynamics of the reaction such that the cyclization reaction becomes faster than the intermolecular hydrogen abstraction,

Scheme 2.9



the use of DMPU was evaluated. Thus, in the attempted cyclization reaction of 1,11–dibromo–undeca–2–yne **164** with bis(cyclopentadienyl)titanium(III) chloride, nine equivalents of DMPU were added to the reaction mixture. Unfortunately, the reaction produced no identifiable products.

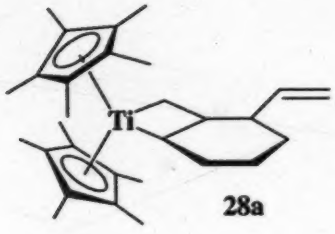
Exactly why such a discrepancy exists between differently substituted Cp series' ability to promote large ring synthesis by intramolecular radical cyclization is unknown.

Differences between the pentamethylcyclopentadienyl and cyclopentadienyl ligand sets in the ability to facilitate intermolecular reactions has already been discussed from an MO perspective: the extra electron richness associated with the pentamethylcyclopentadienyl series[22] may enhance the metal–ligand interaction, increasing ligand stability to the necessary η^3–coordination mode, or destabilize the semi–occupied molecular orbital (SOMO), making it more susceptible to radical attack, or both. Electronic differences alone are unlikely to adequately explain why, for example, in the pentamethylcyclopentadienyl series, a titanacyclobutene complex containing a 12 membered B–ring can be formed, but a compound with a 14 membered B–ring can not. More plausibly, the extra range of motion gained by the addition of two methylene groups in the tether are responsible. At a certain chain length specific to each ancillary ligand set, the entropic advantage gained by the templating effect of the ancillary ligand set becomes outweighed by the inherent entropy of the larger tether length. The additional negative entropy associated with the ordering required to attain bond–forming distances becomes prohibitive. The radical terminus can possibly undergo intermolecular trapping or, more likely, a destructive side reaction with some radicophilic species (e.g., solvent) before intramolecular cyclization can occur. The volume occupied by the pentamethylcyclopentadienyl ligand set[19] is much greater than that occupied by the cyclopentadienyl set, and as such, may restrict the degree of freedom available to the long–chain end of a ligand much more. Because unsubstituted cyclopentadienyl ligands occupy much less volume, the long–chain ligand has much more freedom of motion, and

therefore the entropic advantage is surpassed at shorter chain lengths than in the pentamethylcyclopentadienyl case.

Because of the apparent dependence of ring size formation on the size of the ancillary ligand set, the sterically demanding $(DMAI)_2$–TiCl, **129**, was deemed a reasonable choice for these demanding cyclization reactions. The large profile of the dimethyl amino indenyl system was expected to allow for reasonably large titanabicyclobutene complex synthesis. In the event, however, none of the attempted cyclization reactions employing **129** proceeded to cleanly yield the desired product.

D. Intramolecular Propargyl Radical Cyclizations of Titanium(III) Propargyl Compounds to Form Bicyclic Allenes. In the previous section, intramolecular cyclization reactions by radical attack on bound η^3–propargyl/allenyl ligand were demonstrated by the use of single substrates possessing both ligand and alkylating moieties. The purpose was to demonstrate medium– and large–carbocycle synthesis. These reactions, up to a certain ring size, generally proceed in high yields, offering simple bicyclic structures. By applying the same methodology to more elaborated substrates, greater functionality can be built into the final product. A collection of α,ω–bis–propargyl bromide substrates was synthesized to attempt intramolecular cyclization reactions on titanocene templates, analogous to the one example known from allylic chemistry (see Scheme **1.6** pg. 14).[24]



28a

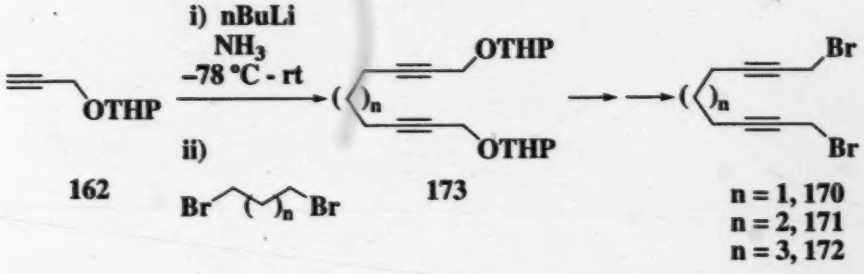
Bicyclic compound **28a** was synthesized by treatment of doubly allylic 1,9–dibromo–2,7–nonadiene with bis(pentamethylcyclopentadienyl)titanium(III) chloride and three equivalents of samarium diiodide (Scheme **1.6**, page 14). Unfortunately, this protocol is sharply limited in allyl chemistry to the construction of the titanabicyclobutane complex with a six–membered B–ring. The reaction is also only known in the pentamethylcyclopentadienyl series: the intramolecular cyclizations using the *tert*–butylcyclopentadienyl and cyclopentadienyl titanocene(III) chlorides do not proceed. The success of radical alkylation chemistry with propargyl substrates[19] where allylic substrates failed[25,28] suggested that the syntheses of compounds analogous to **28** might work within the domain of propargyl/allenyl chemistry, and that a greater variety of ring sizes might be accessible.

i. Substrate synthesis

Substrates **170**, **171**, and **172** were synthesized by the same general procedure as illustrated for 1,11–dibromo–undeca–2,9–diyne **172** (Table **2.6**).[168] Alkylation of the

lithium salt of 2–propynyloxytetrahydropyran (2.3 equivalents) **162** with one equivalent of 1,5–dibromopentane[163] provides the bispropargyl ether (**173**, n = 1) in 88% yield after silica gel chromatography.

Table **2.6** Synthesis of bispropargyl bromide substrates



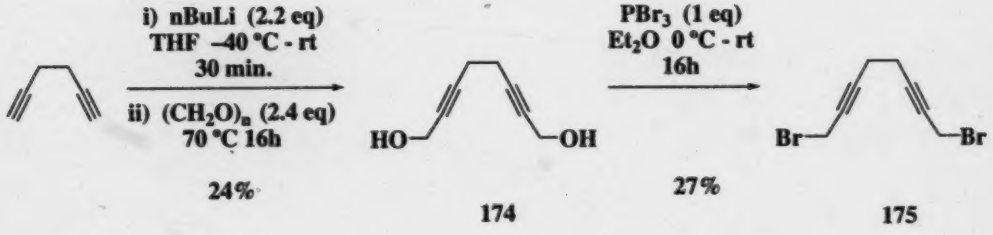
α,ω–bispropargyl product	n	Yield (%) alkylation	Yield (%) deprotection	Yield (%) sulfonate formation	Yield (%) bromide displacement
170	1	77	95	45	99
171	2	97	95	94	90
172	3	88	82	89	99

Deprotection of the THP ethers to afford the bis–alcohol was accomplished by the action of catalytic PPTs in THF/methanol solution at reflux over 16 hours in 82% yield.[169] The 11–hydroxy–2,9–undecadiynol[170,171,172] was next converted to the α,ω bis–toluene sulfonate ester using excess potassium hydroxide and a slight excess of chlorotoluenesulfonate. The bis–toluenesulfonate ester was isolated in 89% yield. Final

conversion to 1,11–dibromo–2,9–undecadiyne **172** was accomplished by displacement of the toluenesulfonate esters using lithium bromide. The bis–propargyl bromide was produced quantitatively and no purification other than filtration to remove the salts was necessary. The overall yield for the four–step synthesis of propargyl substrate **172** is 64%. The shorter substrates **170**[171,172,176] and **171**[171,176] were prepared analogously, using 1,3–dibrompentane and 1,4–dibromobutane, respectively.

The eight–carbon substrate **175**[173] was synthesized by an alternate route (Scheme **2.10**). Homologation of 1,5–hexadiyne was accomplished by deprotonation with n–butyllithium at –40 °C in THF followed by treatment with paraformaldehyde in THF at reflux.[176] The yield of the desired diol **174**[173] was 24%. This bis–propargyl alcohol was converted to the bromide by reaction with phosphorous tribromide.[176]

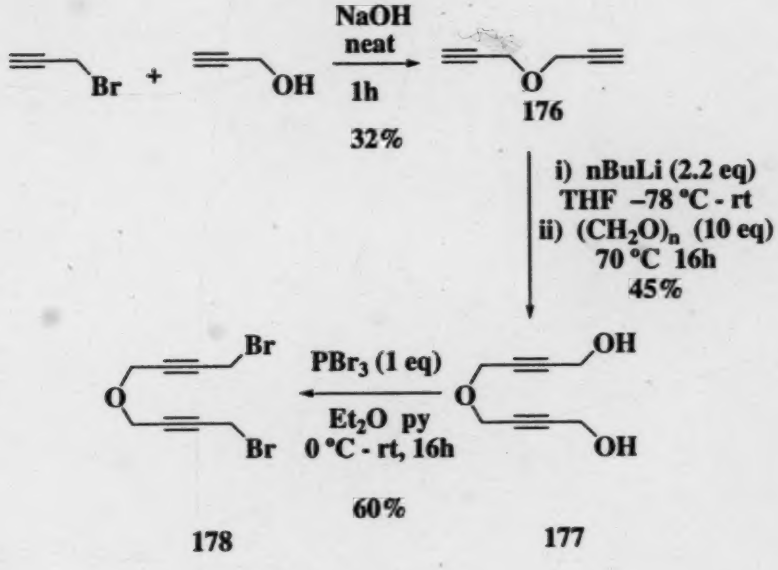
Scheme **2.10**



The synthesis of oxygen–containing nonadiyne substrate **178**[176] was also constructed by a different route than that of carbon–containing analogue **170** (Scheme **2.11**). Propargyl ether **176**[174] was prepared by the reaction of propargyl alcohol, propargyl bromide, and base.[175] The product was purified by distillation. The product

ether, 4–oxa–1,6–heptadiyne **176** was recovered in 32% yield. Bis–alcohol **177** was prepared from ether **176** by n–butyllithium deprotonation and subsequent formaldehyde homologation[176] to yield 4–(4–hydroxy–but–2–ynyloxy)–but–2–yn–1–ol, **177**, in 45% yield as a fluffy off–white powder after recrystallization. Phosphorous tribromide was used to convert diol **177** to the target material.[176] Dibromide **178** was isolated as a colourless oil in 60% yield after silica gel chromatography.

Scheme **2.11**



ii. Results

Products from the reactions of these α,ω–bispropargyl bromide substrates with titanocene(III) chlorides and samarium diiodide are bicyclic titanacyclobutene complexes with an appended allenyl moiety (Scheme **2.12**). Products arise from a formal coupling of two propargyl species in a regiospecific manner, and the reaction offers another

method to circumvent the generally poor regioselectivity associated with organic propargyl–propargyl couplings.[12]

Cyclization reactions with α,ω–bispropargyl substrates were moderately successful in the *tert*–butylcyclopentadienyl ligand series. The general reaction procedure and workup are the same as those previously discussed. The reaction of bis(*tert*–butylcyclopentadienyl)titanium(III) chloride and three equivalents of samarium diiodide with 1,10–dibromo–2,8–decadiyne, **171**, proceeds in 80% yield to afford 8,8–bis(*tert*–butylcyclopentadienyl)titanabicyclo[5.2.0]–2–allenyl–nona–1–(7)–ene **180** (Scheme **2.12**). The *tert*–butylcyclopentadienyl ring hydrogens appear in the ^{1}H NMR spectrum at δ 5.89, 5.62, 5.57, and 5.46 (Table **2.9**). The allene terminal hydrogens (F) appear as a single signal at δ 4.85 in the ^{1}H NMR spectrum (Table **2.9**). The titanacyclobutene ring resonances in the ^{13}C (APT) NMR spectrum are typical: a shift of 219.6 ppm is observed for the α–quaternary carbon (A), 96.2 ppm for the β–carbon (B), and 71.6 ppm for the α–methylene carbon (C). The ^{13}C NMR signals of the allenyl moiety occur at δ 104.1 (D), δ 211.9 (E), and 75.2 (F), and are reasonably characteristic of an allenyl moiety.[177] Spectroscopic assignments were confirmed by correlated spectroscopy. More complete analysis is presented in the Experimental section.

The reaction of 1,9–dibromo–2,7–nonadiyne **170**, with bis(*tert*–butylcyclopentadienyl)titanium chloride and three equivalents of samarium diiodide provided 7,7–bis(*tert*–butylcyclopentadienyl)titanabicyclo[4.2.0]–2–allenyl–octa–1–(6)–ene **181**, in 85% yield (Scheme **2.12**). Some relevant ^{1}H and ^{13}C NMR data are shown in Table **2.7**. An attempt to use 1,11–dibromo–2,9–undecadiyne **172** to form the larger 9,9–

bis(*tert*-butylcyclopentadienyl)titanabicyclo[6.2.0]–2–allenyl–deca–1–(8)–ene does not proceed.

Scheme **2.12**

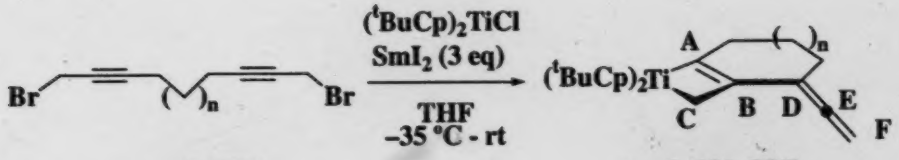


Table **2.7** Selected NMR data for compounds 180, 181, 182

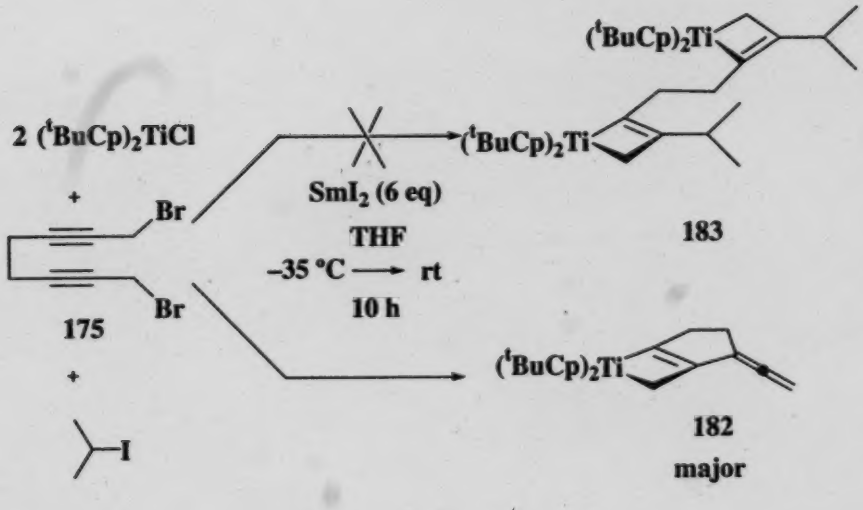
#	$^{1}H_C$ (ppm)	$^{1}H_F$ (ppm)	$^{13}C_A$ (ppm)	$^{13}C_B$ (ppm)	$^{13}C_C$ (ppm)	$^{13}C_D$ (ppm)	$^{13}C_E$ (ppm)	$^{13}C_F$ (ppm)
182	3.41	5.21, 4.92	224.2	97.7	62.8	‡	‡	‡
181	3.21	4.97	220.8	94.3	67.9	100.7	210.4	76.5
180	3.26	4.85	219.6	96.2	71.6	104.1	211.9	75.2

‡: assignments ambiguous

Reaction of 1,8–dibromo–2,6–octadiyne **175** under standard reaction conditions failed to produce the bicyclic allene **182** (Scheme **2.13**). Serendipitously, however, **182**, was obtained as the major product in an attempt to make an entirely different molecule. The reaction of two equivalents of bis(*tert*–butylcyclopentadienyl)titanium chloride, six equivalents of samarium diiodide, one equivalent of **175**, and two equivalents of 2–

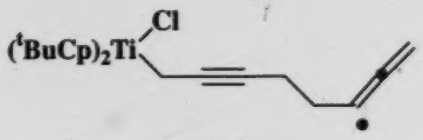
iodopropane was expected to produce tethered di–titanacyclobutane complex **183**. Instead, the ^{1}H NMR spectrum of the crude product mixture was consistent with allenyl bicyclic compound **182**, showing two singlets corresponding to one hydrogen each, at δ 5.41 and 4.82. This is the region typical for the alkene hydrogens of titanabicycloallenyl complexes. A titanacyclobutene core is further suggested by hallmark ^{13}C NMR resonance at δ 224.2, 97.7, 62.8. A comparison of certain spectroscopic data with the 6– and 7–membered B–ring analogs is presented in Table **2.9**. Efforts to produce the five–membered analogue exclusively failed to give a product cleaner than this initial

Scheme **2.13**



synthesis. This failure under the standard reaction conditions is unexpected, as the radical cyclization to form a five–membered ring should be facile. The reason for this may be the same as that for the failure of 1,11–dibromo–2,9–undecadiyne to undergo cyclization to form the ten-membered allenyl compound: namely that intermolecular

processes, probably hydrogen atom abstraction, compete too efficiently with the intramolecular cyclization process. As with the simpler bicyclic cases (Scheme **2.8**, structure **160**, pg. 98), intermediate titanium(IV) compound **184** may be quenched by hydrogen atom before the reduction of the titanium centre and subsequent cyclization can happen. "Protection" of this radical (**184b**, Scheme **2.14**) as a σ–bond to Ti(IV) allows



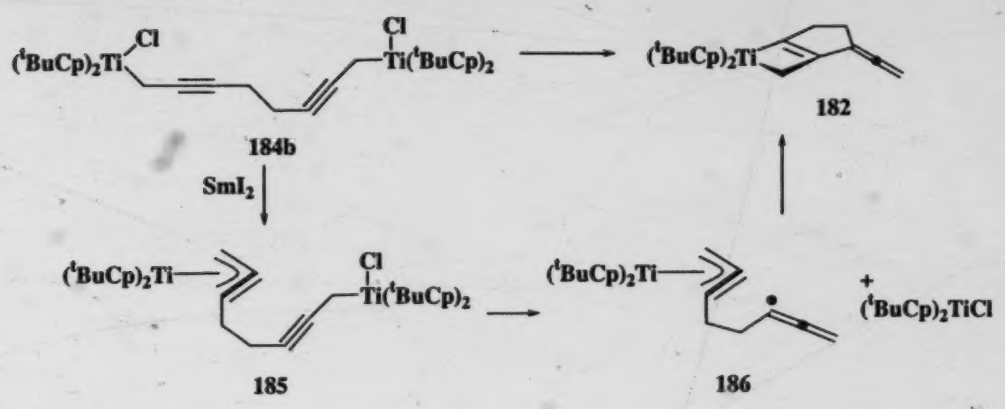
184

the reduction of the titanium centre and formation of the receptive η^3–intermediate **185** to occur before the propargyl radical at the other terminus is ejected,[13] allowing the formation of the bicyclic allene **182**.

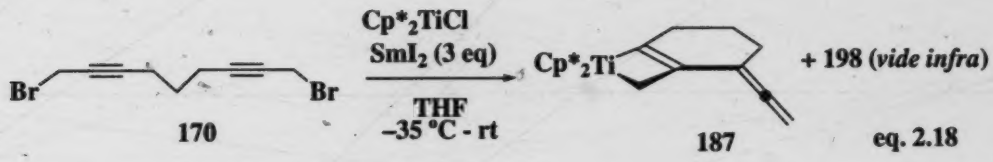
However, the reaction of two equivalents of bis(*tert*–butylcyclopentadienyl)-titanium(III) chloride and three equivalents of SmI_2 with one equivalent of 1,8–dibromo–2,6–octadiyne, **175**, failed to produce 6,6–bis(*tert*butylcyclo-pentadienyl)titanabicyclo[3.2.0]–2–allenyl–hepta–1–(5)–ene cleanly or uniquely.

In the Cp* series, 1,9–dibromo–nona–2,7–diyne **170** was used in an attempt to form 7,7–bis(pentamethylcyclopentadienyl)titanabicyclo[4.2.0]–2–allenyl–octa–1–(6)–

Scheme **2.14**

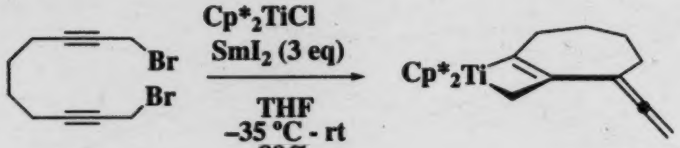


ene **187** (eq. **2.18**). The desired bicyclic compound **187** was formed, but as one of two organo–titanium products. This interesting reaction will be discussed in greater detail in the next section.



However, the higher homologue 1,10–dibromo–deca–2,8–diyne (**171**) reacts with one equivalent of bis(pentamethylcyclopentadienyl)titanium(III) chloride and three equivalents of samarium diiodide to form the bicyclic 8,8–bis(pentamethylcyclopentadienyl)titanabicyclo[5.2.0]–2–allenyl—non–1–(7)–ene **188** in 89% yield (eq. **2.19**). The reaction of the next higher homologue, 1,11–dibromo–undeca–2,9–diyne **172**, with one equivalent of

bis(pentamethylcyclopentadienyl)titanium(III) chloride and three equivalents of samarium diiodide does not proceed to the desired bicyclic titanacyclobutene complex.



171 188 eq. 2.19

The synthesis of the same class of compounds was attempted using the simple *bis*(cyclopentadienyl)titanium(III) chloride. The attempted reaction of bis(cyclopentadienyl)titanium chloride and 1,9–dibromo–2,7–nonadiyne **170** failed to produce any detectable amount of the desired product under standard conditions. Even after extensive heating (80 °C for 72 hours), the reaction solution maintains a blue colour, indicating that the samarium diiodide is not consumed.

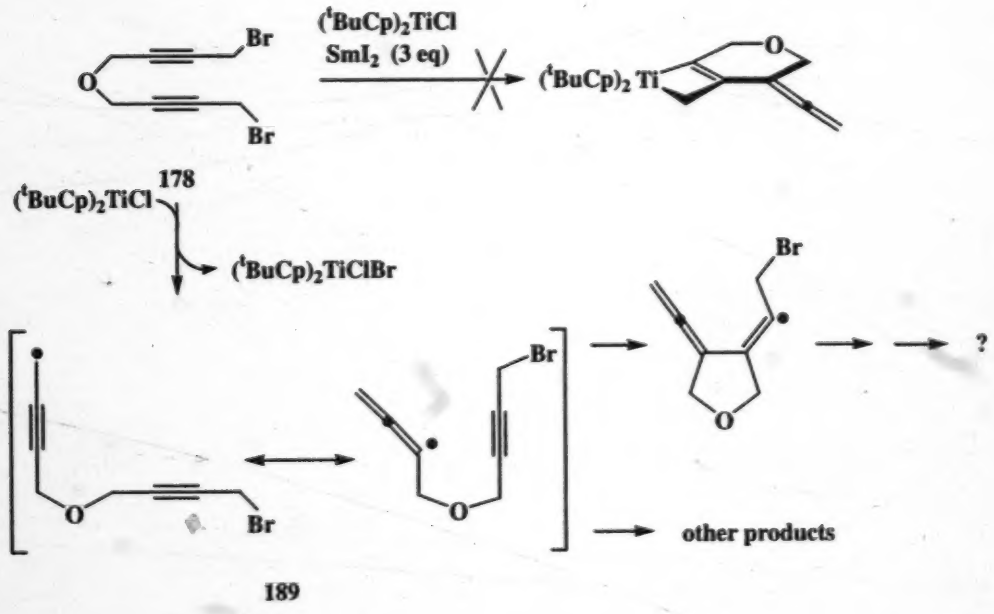
It is difficult to rationalize why the reaction of bis(*tert*–butylcyclopentadienyl)titanium chloride with ten carbon substrate 1,10–dibromo–2,8–decadiyne **171** produces seven–membered ring titanabicyclobutenyl allenyl complex **180** cleanly and with high yields, but reaction with 1,11–dibromo–2,8–undecadine **172** fails to produce even a minor amount of the eight–membered ring bicyclic compound **179** (Scheme **2.12**, page 113). In the *tert*–butylcyclopentadienyl series, the formation of simple ten–membered ring titanabicyclobutene complex **168** (page 104) has already been discussed. In the formation of **168**, the primary radical terminus cyclizes onto the η^3–propargyl/allenyl moiety to form a ten–membered B–ring. In the attempted formation of

the eight–membered allenyl complex **179**, essentially the same reaction pathway must be followed: a propargyl/allenyl radical must "find" the η^3–propargyl/allenyl moiety. If the reaction paths are indeed similar, **179** is expected to form, as the formation of an eight–membered ring is entropically favoured over the formation of a ten–membered ring. The entropic advantage gained by the "templating" effect of the organometallic complex must be reached at shorter chain lengths for the propargyl/allenyl compounds than for the primary alkyl radical compounds. The difference between the two systems must reside in the nature of the alkylating radical. The unstabilized primary radical offers a more efficient radical trap for the odd–electron organometallic species than the more stabilized propargyl/allenyl radical. Alternatively, the bicyclic compound may be formed readily, but reversibly, leading to eventual decomposition products.

One of the objectives of this investigation was to find conditions that allow for the inclusion of synthetically valuable functional groups in the reacting substrates. Attempts to incorporate a heteroatom such as oxygen, however, have been unproductive so far. For example, 1–bromo–4–(4–bromo–but–2–ynyloxy)–but–2–yne, **178**, was constructed as an oxygen–containing analog of 1,9–dibromo–2,7–nonadiyne **170**, which itself undergoes cyclization with bis(*tert*–butylcyclopentadienyl)titanium chloride to form the bicyclic compound **181** (Scheme **2.12**, page 113). Unfortunately, the oxygen–containing substrate **178** does not undergo the same reactivity as the carbon–analogue **170** to form the anticipated product (Scheme **2.15**). A reaction does occur, as evidenced by the rapid discolouration of the reaction solution, but no identifiable products are isolated from the reaction mixture. The reason for this reactivity difference is abstruse: the oxygen atom is

buried as an ether in the centre of the substrate, and should pose no more hazard than the ethereal solvent. Possibly substrate **178** undergoes asynchronous reduction of the two halide atoms, and the propargyl radical **189** presumably results from halide abstraction at one terminus of the molecule. This radical is framed to undergo rapid 5–exo–dig cyclization, and this side reaction may consume the starting material. Although this is possible, the absence of the corresponding reactivity in substrate **170**, as well as the failure to detect furan byproducts suggests strongly that some other process may be occurring.

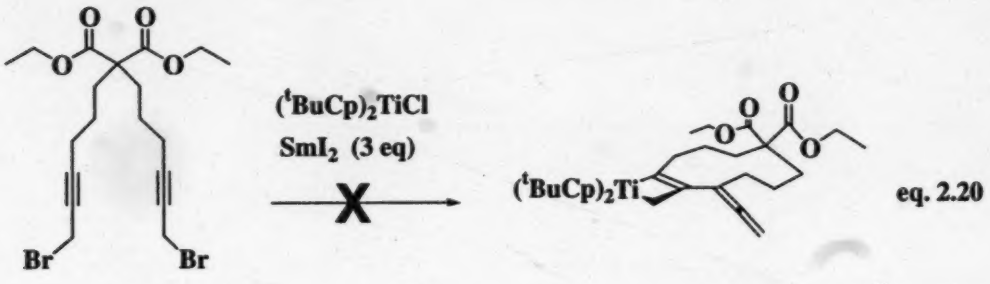
Scheme **2.15**



189

Malonate derivative **190** was synthesized in another attempt to extend the scope of the intramolecular cyclization reactions. Titanabicycloallenyl compounds with B–ring

sizes greater than seven have not been synthesized. The 1,1–bis–ester moiety was expected to provide an additional Thorpe–Ingold type entropic assistance[161] to allow formation of larger ring sizes. Malonate **190** was expected to form bicyclic titanium



190 **191** eq. 2.20

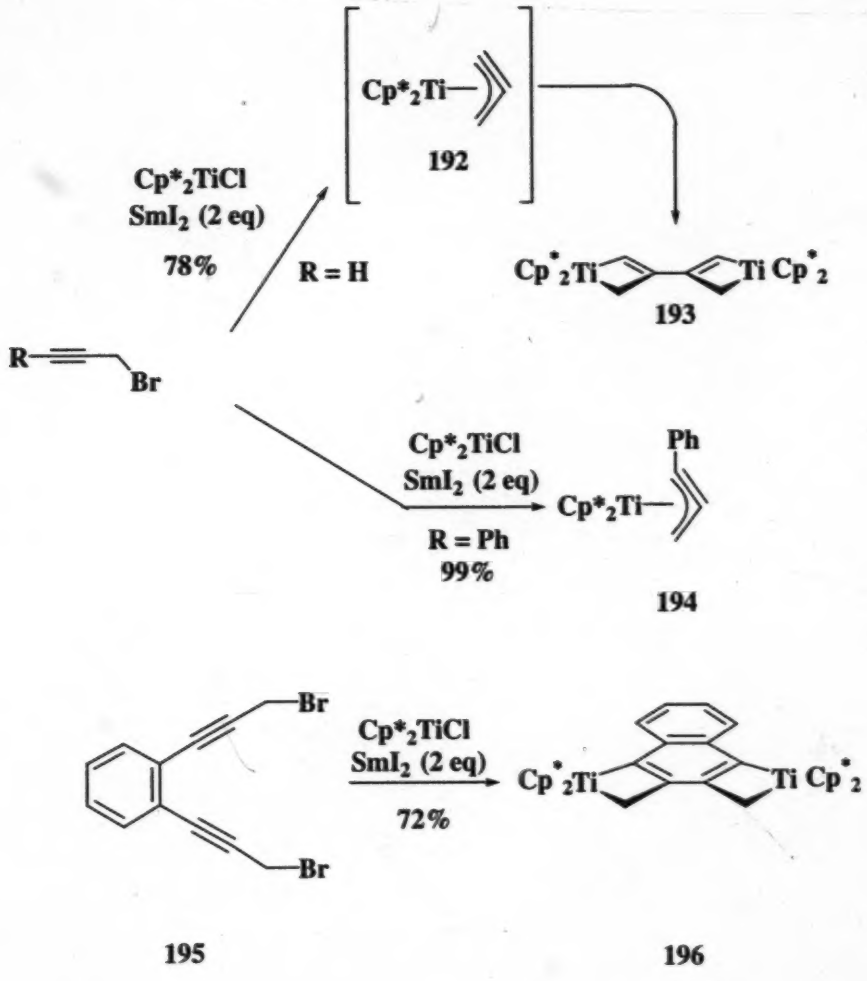
compound **191** (eq. **2.20**), however no discernible organic product was recovered from the reaction.

In summary, only reactions using the *tert*–butylcyclopentadienyl and pentamethylcyclopentadienyl series successfully yield bicyclic allenyl complexes among the titanium templates evaluated. All attempts to synthesize the Cp analogues of compounds **180**, **181**, and **182** (Scheme **2.12**, page 113) failed. The reason for these failures, given that this template works well for other propargyl–based radical chemistry and even intramolecular cyclization reactions, must reside in the nature of the propargyl radical: either its nucleophilicity is too diminished compared to alkyl radicals to add to the π–propargyl titanium moiety, or the addition is reversible, with an unfavourable equilibrium.

E. Intramolecular Ligand–Ligand Coupling of α, ω-Bis(η^3–propargyl)titanium(III) Complexes. Greater insight into the capricious nature of the reactivity of η^3–propargyl/allenyl complexes is gained by considering three of the earliest examples of this chemistry. Ogoshi negotiated an entry into the then–unknown η^3–propargyl/allenyl titanocene(III) structural class by attempting to synthesize the parent propargyl complex, $Cp^*_2Ti(\eta^3–C_3H_3)$ **192** (Scheme **2.16**).[19] Surprisingly, no titanium(III) compound was isolated. Instead the only product formed is the dimeric ligand–ligand coupled dititanacyclobutene product **193**. In contrast, the corresponding reaction using 3–bromo–1–phenylpropyne provides an almost quantitative yield of titanium(III) propargyl complex **194**. No dimerization product was detected. Interestingly, as discussed, 1,2–bis(3–bromopropynyl)benzene **195** undergoes a similar pseudo-dimerization to afford tetracyclic naphthalene derivative **196**. It remained to be determined whether the substrate **195** undergoes ligand–ligand coupling for reasons of entropic opportunity or by gain of resonance energy in the formation of the second aromatic ring.

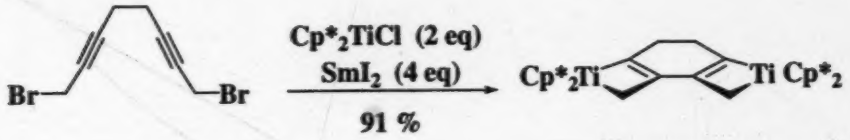
The substrate 1,8–dibromo–2,6–octadiyne **175** was previously discussed for the construction of bicyclic titanacyclobutene complex **182** (Scheme **2.13**, pg. 114) in the bis(*tert*–butylcyclopentadienyl)titanium series. In contrast, when one equivalent of this substrate is added to a –78 °C THF solution containing one equivalent of bis(pentamethylcyclopentadienyl)titanium chloride and four equivalents of samarium

Scheme 2.16



diiodide, tricyclic ligand–ligand coupling product [1,2:3,4–bis(2,2'–bis(pentamethyl-cyclopentadienyl)titanacyclobuteno)]cyclohexadiene **197** is formed in 91% yield (eq. **2.21**). The complex has been characterized spectroscopically, giving data fully consistent with other members of this structural class.[19] Unfortunately, compound **197** is unstable

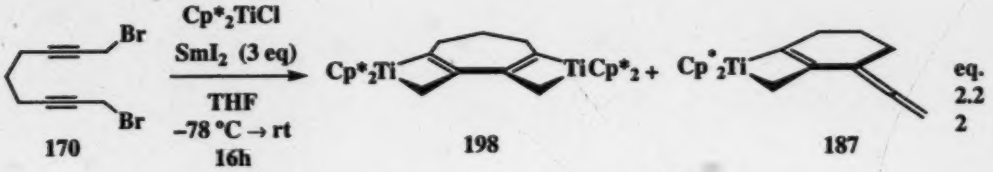
even at –35 °C in solution and all attempts to grow crystals suitable for X–ray analysis failed. The nature of the decomposition process is unknown, but may involve homolysis of the carbon–carbon bond that links the two ligands, the reverse of the radical coupling process.



175 197 eq. 2.21

Other intramolecular ligand–ligand pseudodimerization reactions were attempted. In the previous section, the reaction of one equivalent of 1,9–dibromo–nona–2,7–diyne **170** with one equivalent of bis(pentamethylcyclopentadienyl)titanium chloride and three equivalents of samarium diiodide was described. This reaction leads to a roughly 1:1 mixture of the anticipated bicyclic compound 7,7–bis(pentamethylcyclopentadienyl)-titanabicyclo[4.2.0]–2–allenyl–octa–1–(6)–ene **187** (equation **2.18**, pg. 116) and the tricyclic ligand–ligand coupling product [1,2:3,4–bis(2,2'–bis(pentamethyl-cyclopentadienyl)titanacyclobuteno)]cycloheptadiene **198** (eq. **2.22**). By altering the stoichiometry of the bis(pentamethylcyclopentadienyl)titanium chloride and the samarium diiodide present, the ratio of the products can be altered. When two equivalents of bis(pentamethylcyclopentadienyl)titanium chloride and four equivalents of samarium diiodide are allowed to react with **170** at –78 °C, tricyclic complex **198** and bicyclic allenyl complex **187** are obtained in a ratio of 5:1 (by ^{1}H NMR integration).

Running the reaction at –35 °C with the same stoichiometry leads to a ratio of **198** to **187** of 3:1. Reactions that are started at temperatures above –35 °C do not yield any of the desired product.



170 198 187 eq. 2.2 2

1 : 1

Cp^*_2TiCl (2 eq)
SmI_2 (4 eq)
THF
–78 °C → rt
16h

5 : 1

Cp^*_2TiCl (2 eq)
SmI_2 (4 eq)
THF
–35 °C → rt
16h

3 : 1

By use of excess bis(pentamethylcyclopentadienyl)titanium chloride (four equivalents) and samarium (six equivalents) in THF at –78 °C, the tricyclic dimerization compound **198** was produced in 77% isolated yield (based on 1,9–dibromo–nona–2,7–diyne). In addition to consistent signals in the ^1H NMR spectrum, characteristic titanacyclobutene signals are present in the ^{13}C NMR spectrum. Singlets at δ 218.4, 97.2 and a triplet at δ 80.5 ($^1J_{C-H}$ = 135 Hz) correspond to the titanacyclobutene core. The allylic carbon of the cycloheptadiene ring appears as a triplet at δ 37.6 ($^1J_{C-H}$ = 123 Hz).

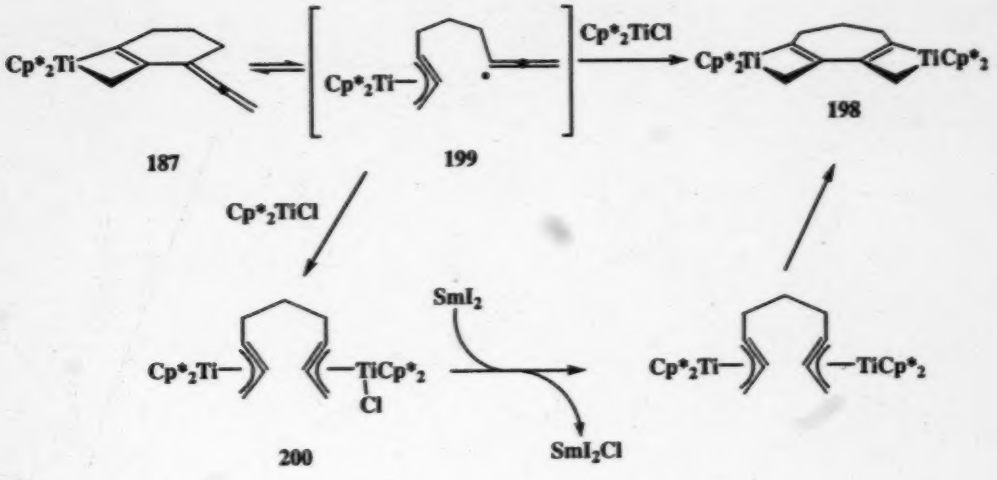
The homoallylic carbon of the cycloheptadiene ring overlaps with the pentamethyl cyclopentadienyl ring methyl quartet at δ 11.8.

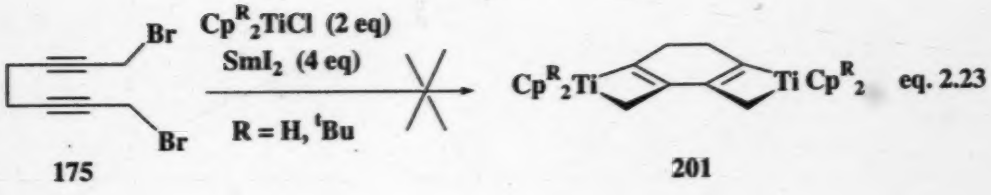
Isomerization of the bicyclic allene complexes was probed as a potential method to convert mixtures of the tricyclic dimerization and bicyclic allenyl species fully to the tricyclic compounds. The product mixtures are unstable even under inert atmosphere, the presumed decomposition mechanism involving carbon–carbon bond homolysis (Scheme **2.17**). If this were the case, the equilibrium concentration of the titanium(III) species **199** should be trapped with bis(pentamethylcyclopentadienyl)titanium chloride to form mixed oxidation state complex **200**. Upon reduction, this species could undergo intramolecular coupling to form the tricyclic complex **198**. To test this supposition, solutions of the mixtures of products were treated with bis(pentamethylcyclopentadienyl)titanium chloride and samarium diiodide and allowed to react at various temperatures and for extended periods of time. Under the reaction conditions tested, however, no conversion or alteration in the product ratio (by ^{1}H NMR spectroscopy) was apparent.

This ligand–ligand coupling reaction, in both intra– and intermolecular fashion, has been observed only using the pentamethylcyclopentadienyl series. To examine whether ligand–ligand coupling is possible in the cyclopentadienyl and *tert*–butylcyclopentadienyl series in an intramolecular manner, bis(cyclopentadienyl)titanium chloride and bis(*tert*–butylcyclopentadienyl)titanium chloride were (independently) mixed with **175** under reaction conditions identical to those used to synthesize **197** (eq. **2.23**). No formation of tricyclic compound **201** was observed in either series. In the

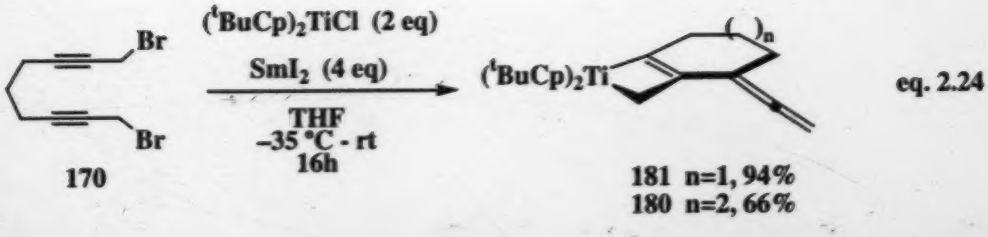
tert–butylcyclopentadienyl series, use of the longer substrates **170** and **171** resulted not in formation of the desired tricyclic compounds, but instead produce cleanly the bicyclic allenyl products **181** and **180** in 94% and 66% yield, respectively (eq. **2.24**).

Scheme **2.17**





eq. 2.23

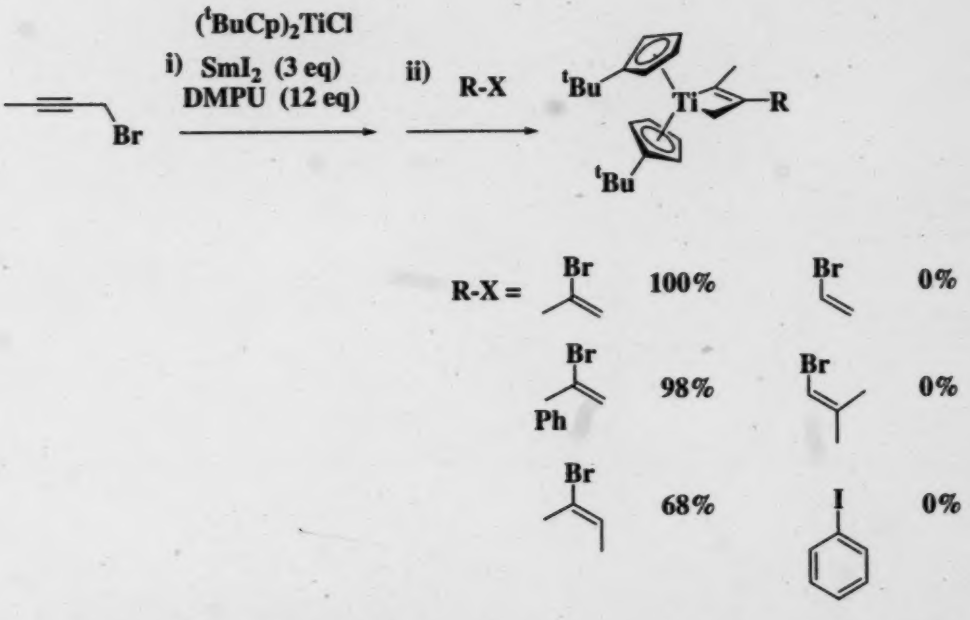


eq. 2.24

F. *Conclusions*

In addition to expanding the scope of intermolecular radical addition reactions for the formation of titanacyclobutene complexes, the use of vinyl radicals to alkylate the *in–situ* derived titanium propargyl complexes was demonstrated and represents a potentially important extension of the methodology that allows for a new class of titanacyclobutene complexes. Vinyl halides α–bromostyrene, 2–bromopropene, and *trans*–2–bromo-2–butene result in the desired titanacyclobutene complexes whereas iodobenzene, vinyl bromide, and 1–bromo–2–methylpropene do not (Scheme **2.18**).

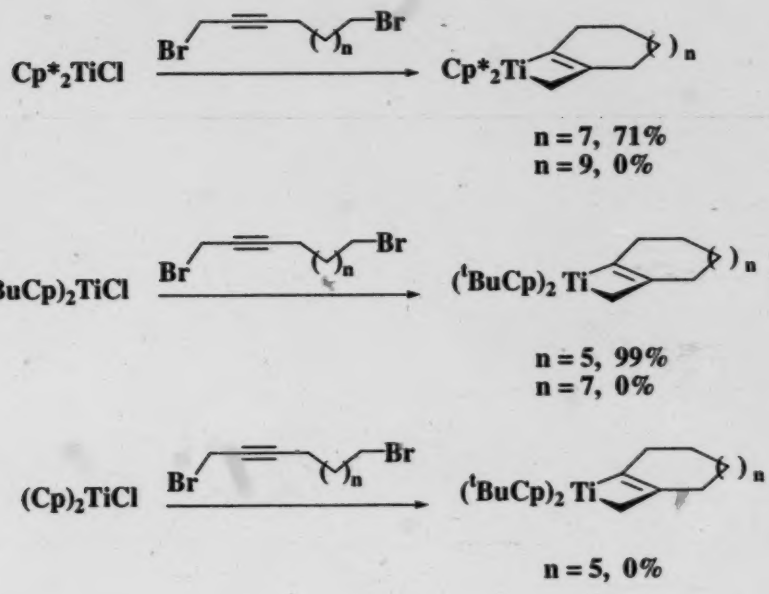
Scheme **2.18**



Also investigated were intramolecular cyclization reactions to form simple bicyclic titanacyclobutene complexes, using α-propargyl-ω-bromo substrates to study the upper limits of ring size attainable using three ancillary ligand sets. We found that ring

sizes as high as twelve are possible with the (pentamethyl)cyclopentadienyl ligand set, but a fourteen-membered ring is not possible, under standard conditions. In the *tert*–butylcyclopentadienyl series, the largest ring size obtained was ten, whereas in the cyclopentadienyl series, not even the ten-membered complex could be obtained (Scheme **2.19**).

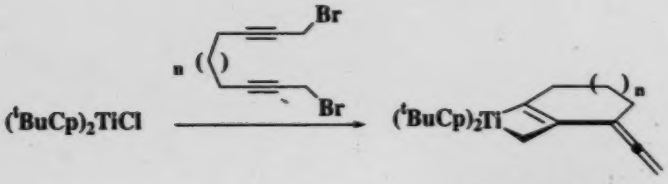
Scheme **2.19**



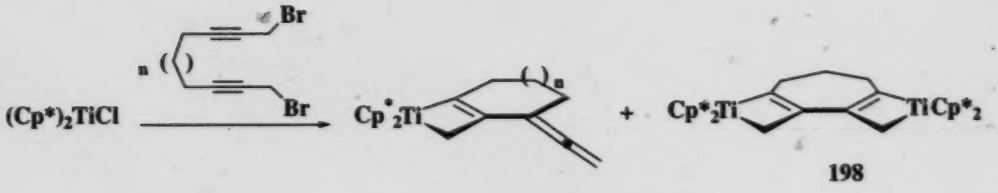
Intramolecular cyclization reactions with α,ω-bispropargyl substrates were also investigated, producing bicyclic allenyl titanacyclobutene complexes. In the *tert*–butylcyclopentadienyl series, ring sizes of five, six, and seven could be obtained (Scheme **2.20**). In the pentamethylcyclopentadienyl ligand set, a ring size of seven was obtained cleanly with 1,10-dibromo-deca-2,8-diyne, but use of 1,9-dibromo-2,7-diyne

resulted in a mixture of the bicyclic allenyl product and the tricyclic bis(titanacyclobutene) complex **198**. Cyclizations in the cyclopentadienyl series do not proceed.

Scheme **2.20**



n = 0, 182 major
n = 1, 181 85%
n = 2, 180 80%
n = 3, 179 0%



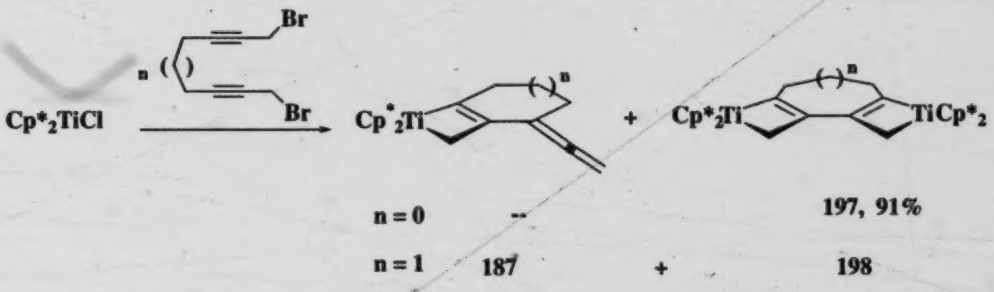
198

n = 2, 184 89%
n = 1, 187, 198

The same class of organic substrates was investigated for the intramolecular ligand-ligand dimerization to form tricyclic bis(titanacyclobutene) complexes. The reaction with 1,8-dibromo-octa-2,6-diyne produces tricyclic complex **197**, but, as noted above, the use of 1,9-dibromo-nona-2,7-diyne produces the tricyclic complex as well as

the bicyclic allenyl complex (Scheme **2.21**). This type of reactivity is only observed in the (pentamethyl)cyclopentadienyl series.

Scheme **2.21**



Conditions under which commonly encountered organic functional groups–for example carbonyl, carboxyl, and amine groups–can be tolerated and incorporated into the titanacyclobutene structure still await discovery.

Chapter 3. *Functionalization of Titanacyclobutene Complexes.*

A. *Nitrile Insertion and Pyridine Formation*

i. Background

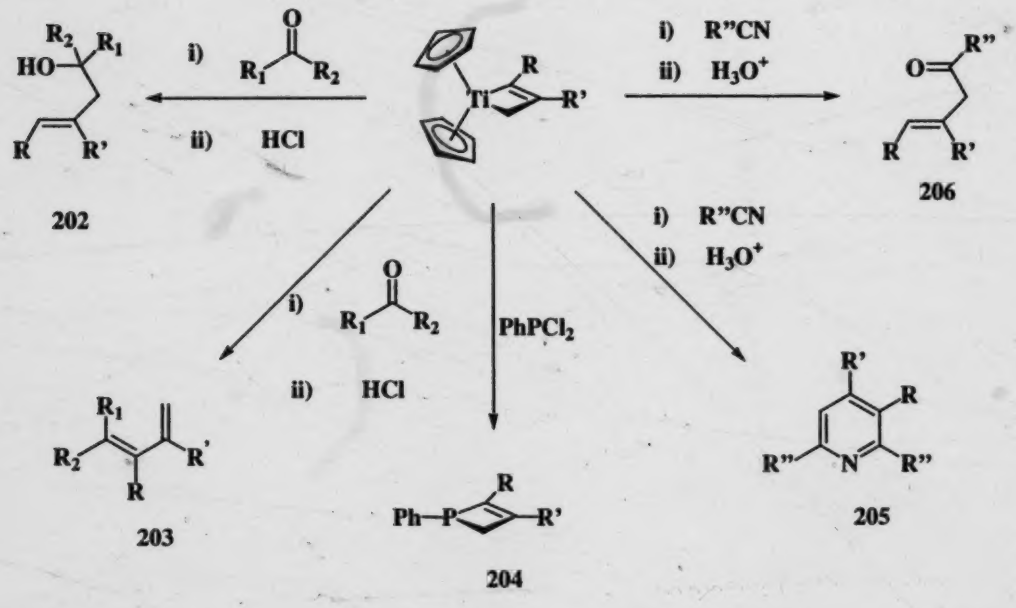
Titanacyclobutene complexes are an interesting class of small molecules that can serve as intermediaries for a variety of useful synthetic transformations. The reactive metal-carbon bonds are capable of incorporating small molecules to become more highly functionalized and, after demetallation, provide various organic compounds. There are a variety of processes documented in the literature for functionalizing titanacyclobutene complexes.[178a,b] In some cases, demetallation of the functionalized compound is spontaneous, in some cases it must be induced. Some of the organic molecules that can be immediately accessed from titanacyclobutenes using known reactions are shown in Figure 3.1 (**202**,[179,180] **203**,[179,180,181] **204**,[182,183,184] **205**,[179,185,186] **206**[179,180]).

As well as influencing the yields of alkylation reactions, the ancillary ligand set has a marked effect on subsequent functionalization of the titanacyclobutene complex: bis(pentamethylcyclopentadienyl)titanacyclobutene complexes are inert to most attempted functionalization reactions, bis(*tert*–butylcyclopentadienyl)titanacyclobutene complexes are resistant, but bis(cyclopentadienyl)titanacyclobutene complexes can be functionalized relatively easily.

Titanacyclobutene complexes react with carbonyl compounds, including aldehydes, ketones, and carbon monoxide, to afford different products. Ketones and

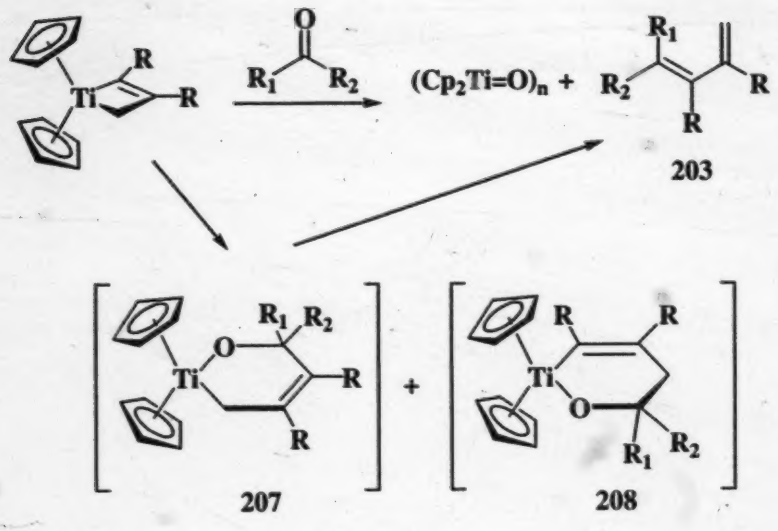
aldehydes preferentially undergo insertion into the titanium–vinyl bond of titanacyclobutene complexes to afford putative titanaoxacyclohexene complexes **207**, but

Figure **3.1**

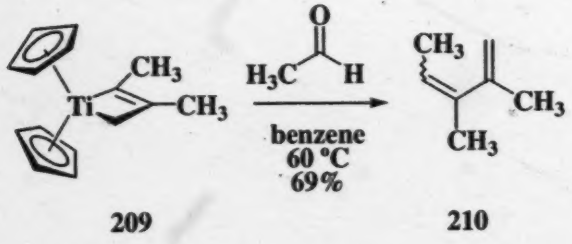


insertion can also be directed into the titanium–alkyl bond (**208**, Scheme **3.1**).[179] Only single insertion products are obtained. Facile thermal decomposition of the oxacyclic intermediate **207** leads to conjugated dienes **203** in synthetically useful yields, perhaps by a concerted retro-[4 + 2] mechanism. For example, addition of one equivalent of acetaldehyde to a benzene solution of 1,1–bis(cyclopentadienyl)–2,3–dimethyl–titanacyclobutene **209** leads to conjugated diene **210** in 69% yield (eq. **3.1**). However, as the steric bulk of either the titanacyclobutene ring substituent (R) or the α–substituents of the ketone or aldehyde (R_1, R_2) increases, an increase in the amount of the titanium–

Scheme 3.1



alkyl-side insertion product is observed (structure **208**, Scheme **3.1**). For example, the reaction of 2,3–diphenyltitanacyclobutene and acetaldehyde leads to a 1:1 mixture of the two insertion products[179] and reaction of 3–methyl–2–phenyltitanacyclobutene with

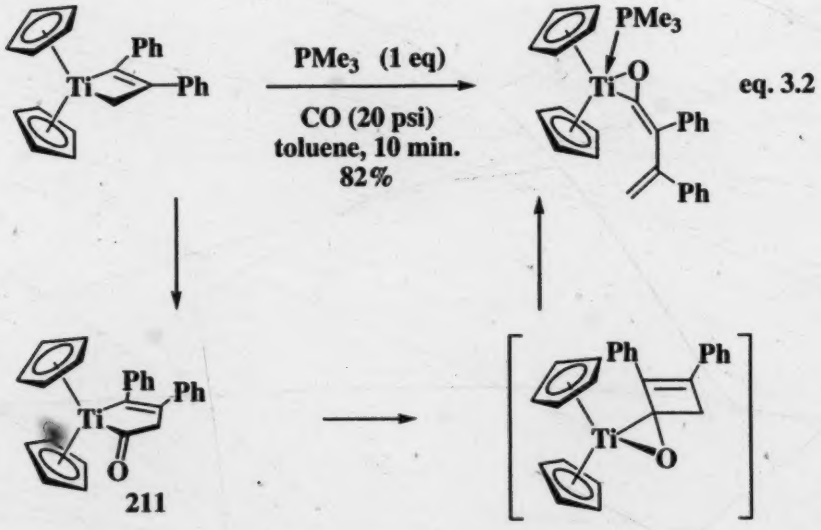


209 **210** eq. 3.1

acetone forms exclusively the titanium–alkyl side insertion product.[180] These alkyl-side insertion products can be readily hydrolyzed using hydrogen chloride gas to afford high yields of the homoallylic alcohols (**202**, Figure **3.1**, pg. 132). A wide variety of ketones,

including conjugated enones have been employed to give homoallylic alcohol products.[180] Esters, carbonates, carbon disulfide, carbon dioxide and imines do not react with titanacyclobutene complexes.[180]

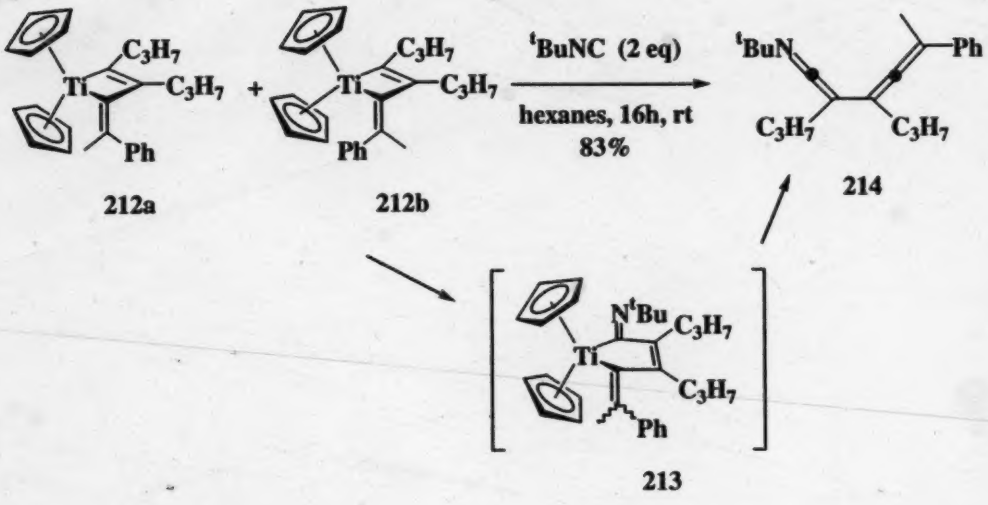
Titanacyclobutene complexes also react with carbon monoxide itself in the presence of a phosphine ligand to afford high yields of the corresponding vinyl ketene adducts (eq. **3.2**).[187] In these cases, the initial insertion is purported to be into the titanium–alkyl bond.



eq. 3.2

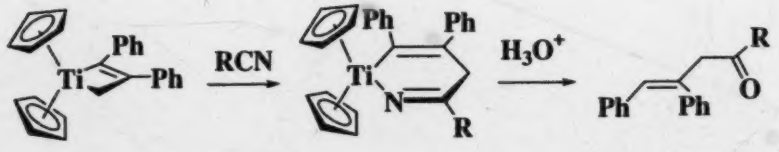
Isonitriles are also reported to react with titanacyclobutene complexes.[187, 130b, 29, 28] A 2:1 mixture of titanacyclobutene complexes **212a** and **212b** in toluene react in the presence of two equivalents of *tert*–butyl isonitrile to afford allenylketenimine **214** in 83% yield, presumably through the intermediacy of complex **213** (Scheme **3.2**).[130]

Scheme 3.2



Another method of functionalizing titanacyclobutene complexes is by reaction with nitriles.[179,180,181,186] These reactions are governed by the two different types of metal–carbon bonds in titanacyclobutene complexes (independent of the ancillary ligand set). Grubbs reports that diphenyltitanacyclobutene undergoes reaction with a variety of nitriles to afford titanaaza–1,5–cyclohexadienes (Scheme 3.3). These

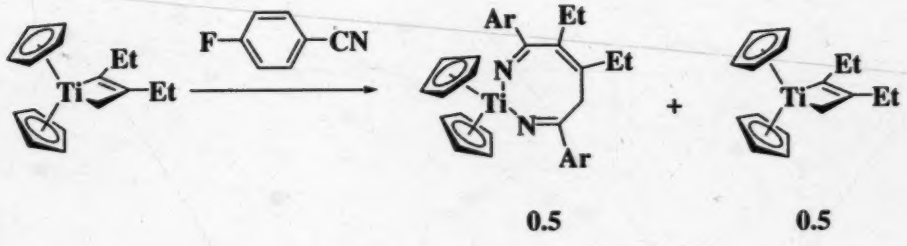
Scheme 3.3



cyclohexadienes are the apparent result of nitrile insertion into the titanium–alkyl bond and can be hydrolyzed to afford ketones.[180] A similar investigation by Doxsee revealed

that the α–substituent on the titanacyclobutene ring affects the reactivity of nitrile insertion. When diethyltitanacyclobutene is used rather than diphenyltitanacyclobutene, the reactivity is altered considerably. For example, in a reaction with only one equivalent of *p*–fluorobenzonitrile, none of the anticipated single insertion product titanaazacyclohexadiene compound was formed (Scheme 3.4). Instead, half of the starting material titanacyclobutene complex remained unreacted, and half incorporated two equivalents of the nitrile.

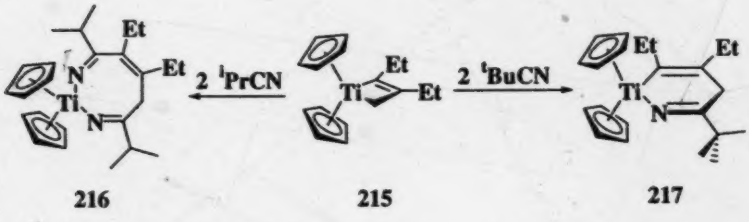
Scheme 3.4



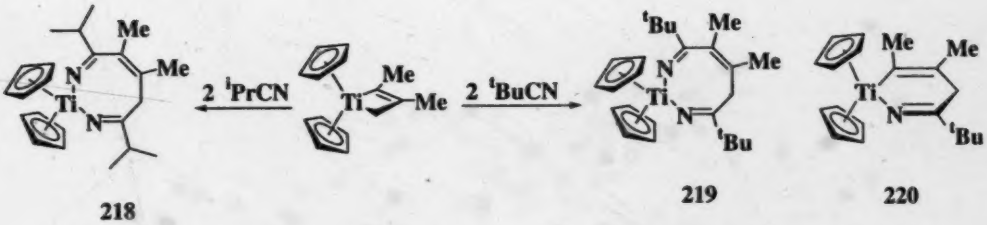
The double insertion products were determined to be the result of apparent insertion of one equivalent of nitrile into the titanium–alkyl bond and one equivalent into the titanium–vinyl bond.[179] As a consequence, a survey of reactions with various titanacyclobutene compounds with various nitriles was undertaken. Analysis of the insertion products, coupled with Grubbs' observation that titanacyclobutene complexes with α–phenyl substituents only give products resulting from single insertion to the alkyl side, suggests that the reactions are sensitive to steric effects; the bulk of both the α–substituent of the titanacyclobutene and of the incoming nitrile influence the reaction

pathway.[179,186] For example, 1,1–bis(cyclopentadienyl)–2,3–diethyltitanacyclobutene **215** reacts with two equivalents of isobutyronitrile to afford mainly the double-insertion product **216** (Scheme **3.5**). Employing pivalonitrile, however, reverses the selectivity of the reaction to afford mainly the single insertion product, **217**.

Scheme **3.5**

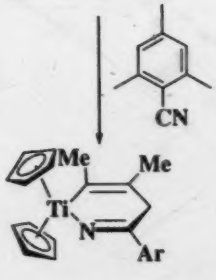


216 **215** **217**



218 **219** **220**

3 : 2



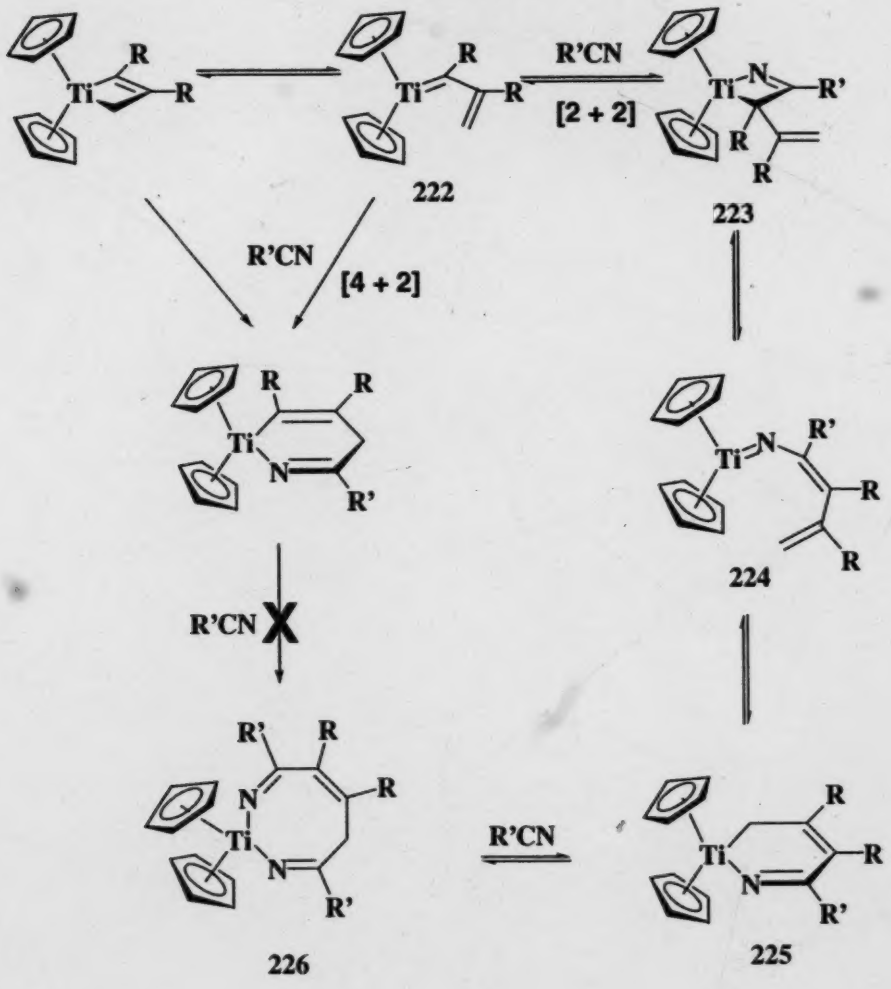
221

Dimethyltitanacyclobutene also undergoes reaction with two equivalents of isobutyronitrile to afford the double insertion product **218** almost exclusively, but upon

reaction with pivalonitrile, gives a 3:2 mixture of double insertion and single insertion products **219** and **220**. When dimethyltitanacyclobutene is treated with the even bulkier 2,4,6–trimethylbenzonitrile, only the alkyl side single insertion product **221** is formed.[185] Treatment of a mixture of single and double insertion titanacyclobutene products with excess nitrile for prolonged periods does not alter the ratio of compounds. This seems to indicate that double insertion product arises from a different reaction pathway than the single insertion product, and not by the sequential reaction of the observed single insertion product with an additional equivalent of nitrile. Doxsee speculates that insertion into the titanium–sp^2 carbon bond is favoured over insertion into the titanium–sp^3 carbon bond, except in cases where it is sterically prohibited.[185] The double insertion products then arise *via* the intermediacy of this single insertion product **225** (Scheme **3.6**), which is formally the result of insertion of nitrile into the titanium–sp^2 carbon bond ("vinyl" insertion).[179] This putative intermediate is very reactive: it has never been isolated. A proposed sequence of events that involves a pericyclic cascade rather than direct migration of a titanium sp^2 bond to a bound nitrile is shown in Scheme **3.6**.[185] Electrocyclic ring opening of a titanacyclobutene complex is proposed to afford vinyl carbene complex **222**.[129] Vinyl carbene **222** can either undergo [4+2] cycloaddition with nitrile to afford single insertion product, or undergo [2+2] cycloaddition with nitrile[188] to afford azatitanacyclobutene **223**. This, in turn, is proposed to undergo electrocyclic ring opening[189] to butadienylimido complex **224**. Butadienylimido **224** may undergo electrocyclic ring closure to titanaazacyclohexa–1,3–diene **225**, which then rapidly coordinates and inserts a second equivalent of nitrile *via* migration of the titanium sp^3

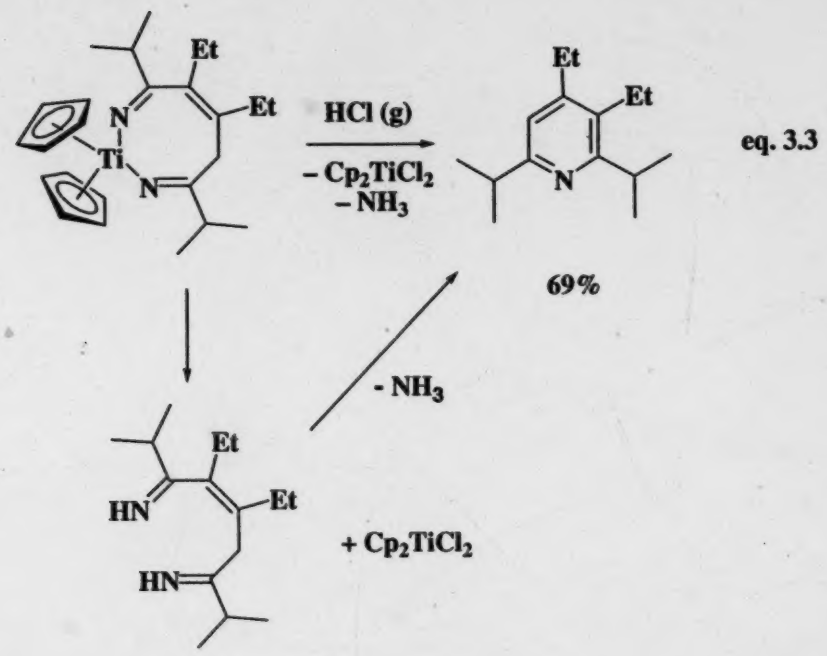
carbon bond. Alternatively, the butadienylimido complex **224** could, in principle coordinate nitrile, and yield the diazatitanacyclooctatriene **226** directly.

Scheme 3.6



As further confirmation of the carbon connectivity of the double insertion products, Doxsee treated them with dry HCl, expecting to isolate corresponding diketones analogous to the single insertion chemistry.[180] Rather than finding diketones,

however, only pyridines were isolated (eq. 3.3).[186] The pyridines are most likely the result of acid– catalyzed cyclization of the diimine or diiminium species formed as the initial product of the reaction of double insertion product with HCl. Bis(cyclopentadienyl)titanium dichloride is also recovered from the reaction mixtures. The tetra–substituted pyridines formed contain two alkyl groups originating from the nitrile, and two originating from the titanacyclobutene complex. The titanacyclobutene complexes employed by Doxsee for these studies were constructed by the reaction of alkyne with Tebbe's reagent.[186] Due to the lack of control over the orientation of the alkyne with the titanium methylidene complex, and therefore the lack of control over the resulting product mixture, only symmetrical alkynes were used. The titanacyclobutenes formed by these reactions necessarily have identical substituents on the α and β positions. As such, the pyridines that result from these titanacyclobutenes have a maximum diversity of two *pairs* of substituents. As a route for constructing pyridines then, this methodology is also limited in the nitrile insertion phase. The substituents in the 2 and 6 position in the pyridine originate from the nitrile, and because of the fast dynamics of the presumed double insertion mechanism, it seems unlikely that the incorporation of two different substituents by controlled insertion of two different nitriles would be possible. However, it is possible to increase the diversity of the pyridines produced by this method by employing titanacyclobutene complexes with different α and β substituents, such as those previously discussed.

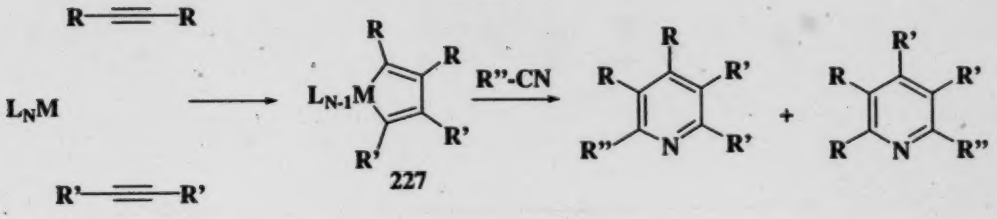


eq. 3.3

Pyridines and molecules that incorporate a pyridine nucleus are ubiquitous in natural product and medicinal chemistry[190] and are employed as building blocks in supramolecular chemistry.[191a] Most conventional methods for constructing highly substituted pyridines suffer low or moderate yields.[191] Transition metal mediated syntheses by co-cycloaddition of two alkynes and one nitrile have been developed.[192] These syntheses are generally regarded as proceeding *via* a metallacyclopentadiene intermediate **227**, which reacts with nitrile to form two regioisomers of pyridine (Scheme **3.7**). Regioselectivity is not controlled in the reaction of the metallacyclopentadiene with nitrile, and so reactions in which two different, symmetrical alkynes have been used afford a mixture of regioisomers. If the alkynes themselves are asymmetrical, six regioisomers may be possible, precluding this method from general synthetic use. The

union of titanacyclobutene complex formation *via* regioselective central carbon radical alkylation with nitrile insertion chemistry can potentially provide a new route to these heavily substituted pyridines.

Scheme 3.7

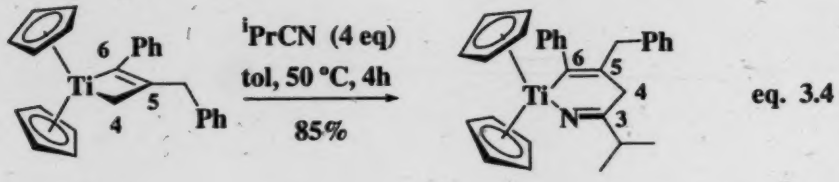


227

ii. Results

a. Single insertion reactions In accordance with Doxsee's observation of nitrile insertions, we also find that titanacyclobutene complexes with an α–phenyl substituent only incorporate one nitrile, with one exception, despite the addition of an excess of nitrile. For example, when 1,1–bis(cyclopentadienyl)–3–benzyl–2–phenyltitanacyclobut-2-ene **107** is heated in toluene with four equivalents of isobutyronitrile, only single insertion product 1,1–bis(cyclopentadienyl)–5–benzyl–3–isopropyl–6–phenyl–2–aza-titanacyclohexa–2,5–diene **228** is produced, in high yield (eq. **3.4**). The depicted connectivity of the molecule is confirmed by spectroscopic analysis. In the ^{1}H NMR spectrum of the product, the C4 hydrogens, originally the methylene group of the parent titanacyclobutene complex, move only very slightly very upfield in the product, to δ 3.11 from δ 3.13. The benzyl hydrogens in the insertion product are shifted slightly downfield

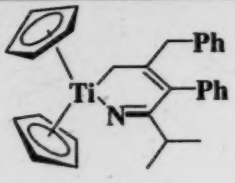
from the parent titanacyclobutene, at δ 3.33 ppm from δ 3.25. However, the changes in ^{13}C NMR shifts are much greater. Upon nitrile insertion, the quaternary carbon α to the titanium centre, C6, shifts upfield from 209.9 ppm to 188.3 ppm. The resonance of the methylene carbon C4 also shifts upfield from 75.5 to 53.8 ppm. The resonance of C5 shifts downfield 30 ppm from δ 96.3 to δ 126.7. A comparison of selected ^{13}C NMR resonances between the parent titanacyclobutene complex **215** and the single insertion product **228** is shown (eq. **3.4**). For clarity of comparison, the numbers shown on the parent titanacyclobutene are those of the corresponding carbon in the insertion product.



eq. 3.4

215 **228**

	$^{13}C3$ (ppm)	$^{13}C4$ (ppm)	$^{13}C5$ (ppm)	$^{13}C6$ (ppm)	$^{13}C7$ (ppm)	$^{13}C12$ (ppm)	$^{13}C13$ (ppm)	$^{13}C(Cp)$ (ppm)
107	–	75.5	96.3	209.9	37.1	–	–	111.5
228	171.3	53.8	126.7	188.3	41.4	35.2	20.0	110.3

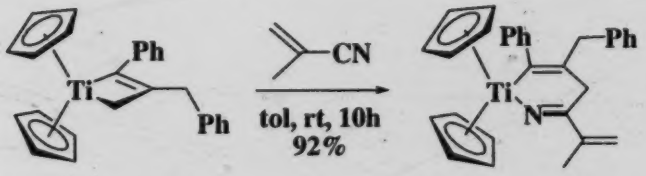


229

Insertion into the metal–alkyl bond to afford product **228** is confirmed by the appearance of a correlation of H4 to C3 in the HMBC spectrum. If insertion occurs into the metal–

vinyl bond (structure **229**) no corresponding HMBC correlation would be apparent because the associated coupling would likely be fully diminished over the four–bond distance. Comprehensive spectroscopic analysis is presented in the Experimental section (Chapter Four).

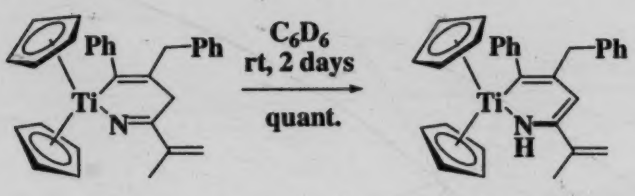
Insertion reactions generally do not require an excess of nitrile to be high yielding. For example, isopropenylnitrile forms clean single insertion product 1,1–bis(cyclopentadienyl)–5–benzyl–3–isopropenyl–6–phenyl–2–azatitanacyclohexa–2,5–diene **230** upon treatment with equimolar titanacyclobutene complex **107**, in high yield at room temperature (eq. **3.5**).



107 **230** eq. 3.5

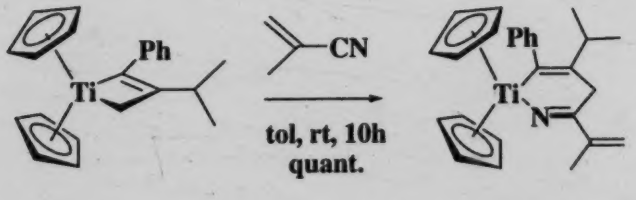
Curiously, insertion product **230** undergoes a spontaneous isomerization even under inert atmosphere in C_6D_6. Over a two–day period, the brownish–red solution of **230** becomes bright green. Spectroscopic analysis suggests that it isomerizes cleanly to the conjugated system 1,1–bis(cyclopentadienyl)–5–benzyl–3–isopropenyl–6–phenyl–2–azacyclohexa–3,5–diene **231** (eq. **3.6**). Although the amino hydrogen could not be identified in the ^{1}H NMR spectrum, other signals are suggestive: the ^{13}C resonance of C4 changes from δ 53.8 ppm to δ 115.5 ppm. The two–hydrogen singlet corresponding to

H4 disappears, replaced by a one–hydrogen singlet at δ 5.90 ppm. IR spectroscopy, which should be diagnostic for the N–H bond, failed in this case to provide a N–H vibrational mode. In a very similar example, however, the N–H bond is clearly observed (Scheme **3.8**, page 147). Assignments are confirmed by correlated spectroscopy, and are presented in detail in the Experimental section (Chapter Four).



230 **231** eq. 3.6

Another single insertion product, 1,1–bis(cyclopentadienyl)–5–isopropyl–3–isopropenyl–6–phenyl–2–azatitanacyclohexa–2,5–diene **232,** was prepared by the reaction of 1,1–bis(cyclopentadienyl)–4–isopropyl–3–phenyltitanacyclobutene with 1.1 equivalents of isopropenylnitrile at room temperature in quantitative yield (eq. **3.7**). Though structurally similar to **230**, no isomerization is observed at room temperature.

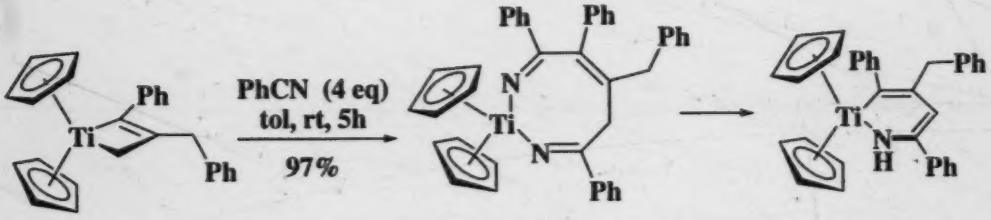


127 **232** eq. 3.7

Despite the general observation that titanacyclobutene complexes with α–phenyl substituents do not undergo double nitrile insertion,[186] an interesting and unique exception to this rule occurs in the reaction of 1,1–bis(cyclopentadienyl)–3–benzyl–2–phenyltitanacyclobutene with excess benzonitrile. This reaction proceeds at room temperature to afford double insertion product 1,1–bis(cyclopentadienyl)–5–benzyl–3,4,7–triphenyl–2,8–diazatitanacycloocta–2,4,7–triene, **233**. This compound is not stable however, and over a 12–hour period at room temperature the molecule extrudes one equivalent of benzonitrile, accompanied by a colour change from brown–red to dark green. The new product is determined spectroscopically to be 1,1–bis(cyclopentadienyl)–5–benzyl–3,6–diphenyl–2–azatitanacyclohexa–3,5–diene **234** (Scheme **3.8**). The ephemeral bis–insertion complex 1,1–bis(cyclopentadienyl)–5–benzyl–3,4,7–triphenyl–2,8–diazatitana-cycloocta–2,4,7–triene **233** is confirmed by NMR data. In the ^{1}H NMR spectrum, consistent aromatic hydrogen signals are accompanied by a singlet at δ 3.70 for the ring methylene hydrogens, and a singlet at δ 3.38 for the benzylic hydrogens. In the ^{13}C APT NMR spectrum, eight downfield quaternary carbon peaks appear at δ 188.4, 161.3, 156.5, 154.9, 154.8, 143.6, 143.6, and 136.2, corresponding to the four *ipso* aromatic carbons and the four alkenyl carbons. Two upfield secondary carbons appear at δ 51.8 and 41.6. Over the acquisition time for the ^{13}C NMR spectrum, peaks from the extrusion product **234** start to appear. Six–membered ring 1,1–bis(cyclopentadienyl)–5–benzyl–3,6–diphenyl–1–azatitanacyclohexa–3,5–diene **234** is confirmed by ^{1}H and ^{13}C NMR spectroscopy, FTIR spectroscopy, and by the high resolution mass spectrum. The

vinylic ring hydrogen appears as a doublet at δ 6.10 (J = 1.2 Hz), possibly coupled to the amine hydrogen. The amine hydrogen is not discernible in the ^{1}H NMR spectrum, and shows no correlation by N–H HSQC spectroscopy. It is readily apparent by IR spectroscopy, however, manifest as a medium–intensity peak at 3341 cm^{-1}. Complete characterization is presented in the Experimental section (Chapter Four).

Scheme 3.8

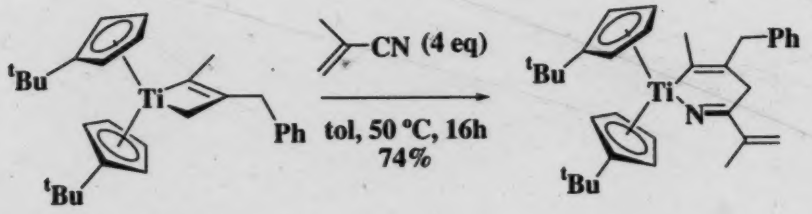


233 234

Titanacyclobutene complexes in the *tert*–butylcyclopentadienyl ligand series are generally more recalcitrant towards functionalization, but are capable of undergoing nitrile insertion. In the cyclopentadienyl ligand series, double nitrile insertion occurs to afford the double–insertion products unless the α–substituent on the titanacyclobutene ring is phenyl, in which case single insertion generally occurs into the metal–alkyl bond exclusively.[185] However, with reactions in the *tert*–butylcyclopentadienyl series, only single insertion into the titanium–alkyl bond is observed. As in the cyclopentadienyl series, further reaction of these single insertion products with excess nitrile does not occur,[185] which precludes bis(*tert*–cyclopentadienyl)titanacyclobutene complexes from serving as pyridine synthons. Single nitrile insertion into the bis(*tert*–

butylcyclopentadienyl)titanium series of titanacyclobutene complexes afford the same "alkyl–side" insertion product as with the bis(cyclopentadienyl)titanium single insertion products; single insertion products in both series presumably arise from the same insertion mechanism.

To illustrate, 1,1–bis(*tert*–butylcyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene **109** reacts with isopropenylnitrile at 50 °C over a sixteen hour period to afford 1,1–bis(*tert*–butylcyclopentadienyl)–5–benzyl–3–isopropenyl–6–methyl–1–azatitanacyclo-hexa–2,5–diene **235** in good yield (eq. **3.8**). Selected ^{13}C NMR data is given in Table **3.1** along with data from cyclopentadienyl–series single insertion product **230** for comparison. Assignments are confirmed by correlated spectroscopy.



eq. 3.8

109 **235**

Further, bicyclic 8,8–bis(*tert*–butylcyclopentadienyl)titanabicyclo[5.4.0]–9–aza–10–phenylundeca–1–(7)–9–(10)diene **237** is formed in 56% yield by the reaction of two equivalents of benzonitrile with 8,8–bis(*tert*–butylcyclopentadienyl)titanabicyclo[5.2.0]-non–1–(7)–ene[28] **236** in toluene at 60 °C (equation **3.9**).

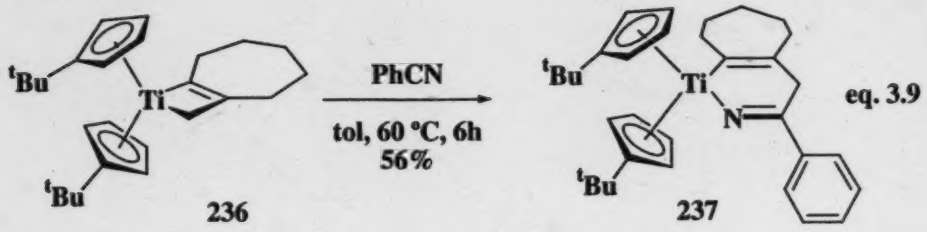
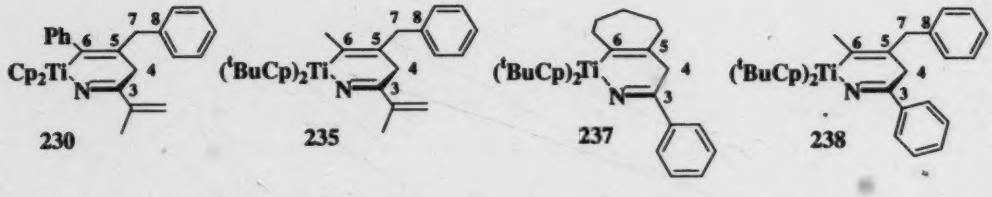


Table **3.1** Comparison of spectroscopic data of compounds **230, 235, 237, 238**

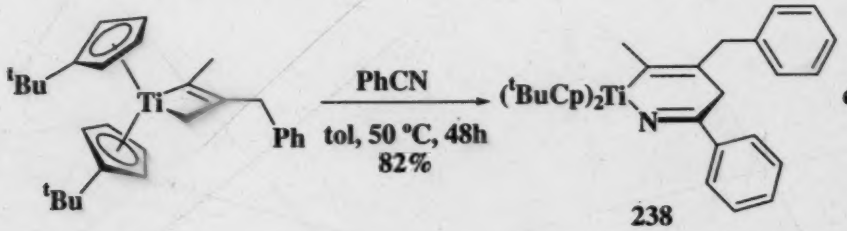


compound	^{13}C NMR (ppm)					
	C3	*C4*	*C5*	*C6*	*C7*	*C8*
230	163.6	50.8	127.2	187.8	41.6	143.6
235	165.7	53.9	126.1	181.7	38.3	142.8
237‡	163.0	57.3	129.2	188.4	–	–
238	163.1	54.2	125.8	182.3	38.4	142.8

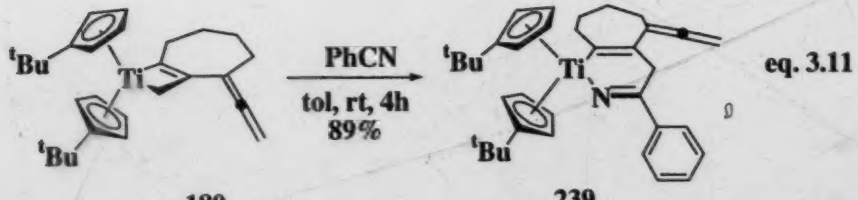
‡: assignments for **237** are made by analogy to similar compounds, and are not confirmed by correlated spectroscopy

As well, 1,1–bis(*tert*–butylcyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene reacts with benzonitrile at 50 °C over a two–day period to afford 1,1–bis(*tert*–butylcyclopentadienyl)–5–benzyl–6–methyl–3–phenyl–1–azatitanacyclohexa–2,5–diene **238** (eq. **3.10**). The compound is not indefinitely stable even under inert atmosphere, decomposing over a period of days at room temperature to an unidentifiable mixture.

Finally, single nitrile insertion was also demonstrated on one of the bicyclic allenyl compounds in the bis(*tert*–butylcyclopentadienyl) series. One equivalent of benzonitrile inserts into 8,8-bis(*tert*–butylcyclopentadienyl)titabicyclo[5.2.0]-2-allenyl-non-1-(7)-ene **180** to afford 8,8-bis(*tert*–butylcyclopentadienyl)titabicyclo[5.4.0]-2-allenyl-9-aza-10-phenyl-undeca-1(7)-9(10)-diene **239** (eq. **3.11**), spectroscopically analogous to compounds **235**, **237**, and **238**.



238 eq. 3.10

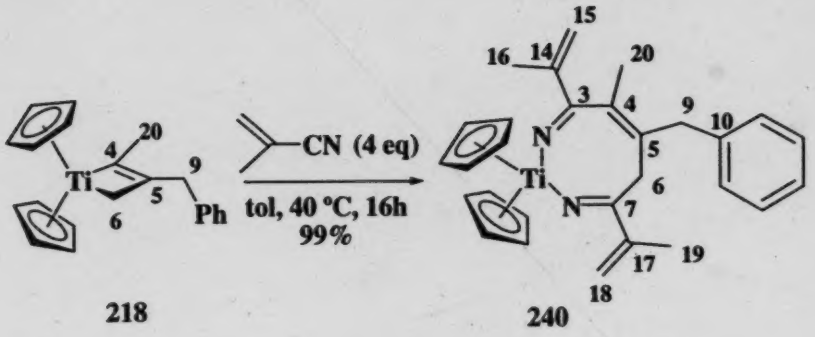


180 **239** eq. 3.11

b. Double nitrile insertion reactions. An illustration of the effect the α–substituent has on nitrile insertion is provided by comparing the reactions of isopropenylnitrile with α–phenyl substituted 1,1–bis(cyclopentadienyl)–3–benzyl–2–phenyltitanacyclobutene **215** and α–methyl substituted 1,1–bis(cyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene **218** (eq. **3.12**). As noted in equation **3.5** (page 144), α–phenyl substituted titanacyclobutene complex **215** incorporates only one equivalent of isopropenyl nitrile to form substituted cyclohexadiene **230** as the only observed product. Interestingly, however, α–methyl substituted **218** incorporates two equivalents of isopropenyl nitrile to form 1,1–bis(cyclopentadienyl)–5–benzyl–3,7–diisopropenyl–6–methyl–2,8–diazatitanacycloocta–2,5,7–triene **240** exclusively; none of the single insertion product is found. This is consistent with the reactivity noted by Doxsee for similar systems.[179] Pertinent NMR data for complex **240** are shown in Table **3.2**. For clarity, the atom labels of starting material **218** are those corresponding to product **240**. The equivalent C6 hydrogens of titanacyclobutene **218** become inequivalent in the product **240**, appearing as two doublets at 3.30 and 3.12 ppm. Similarly, the C9 hydrogens, equivalent in the starting material, appear as two doublets at 3.56 and 3.24 ppm. Both inequivalencies are presumably the result of conformational constraints of the puckered eight-membered ring at ambient temperature. Not all assignments can be made definitively; those that appear in Table **3.2** have been confirmed by correlated spectroscopy. The mass could not be confirmed by electron–impact mass spectroscopy as no corresponding parent *m/z* peak was visible.

Two additional examples of nitrile insertion were observed with 1,1–bis(cyclopentadienyl)–3–benzyl–4–methyltitanacyclobutene **218**. In the presence of a large excess, two equivalents of isobutyronitrile are incorporated into **218** to form 1,1–bis(cyclopentadienyl)–5–benzyl–3,7–diisopropyl–6–methyl–2,8–diazatitana-cycloocta–2,5,7–triene **241** in 86% yield (Table **3.3**). The reaction of **218** with excess benzonitrile affords 1,1–bis(cyclopentadienyl)–5–benzyl–6–methyl–3,7–diphenyltitanacyclo–2,8–di-azaocta–2,4,7–triene **242** in 77% yield. Additionally, titanacyclobutene 1,1–bis(cyclopentadienyl)–3–benzyl–4–phenyltitanacyclobutene **215** was found to form a double insertion product in the reaction with excess benzonitrile: 1,1–bis(cyclopentadienyl)–5–benzyl–3,4,7–triphenyl-titanacyclo–2,8–diaza-octa–2,4,7–triene **233** was obtained in 97%.

The product diazatitanacyclooctatrienes are all similar spectroscopically with respect to ^{13}C NMR spectral data, displaying comparable chemical shifts for the ring and Cp carbons. The inequivalencies of the C6 and C9 hydrogens discussed above for compound **240** are also observed for the benzonitrile-derived product **242** (Table **3.3**). However, compounds **233** and **241** display only singlets for the C6 and C9 hydrogens. Data is presented in the Experimental section (Chapter Four).

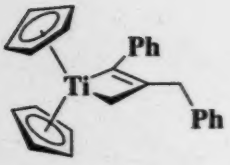
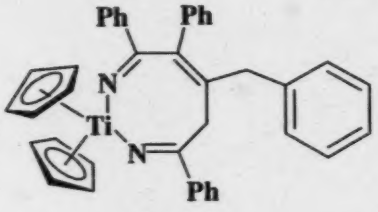
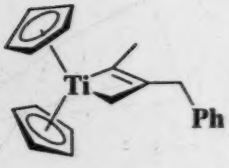
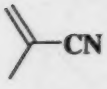
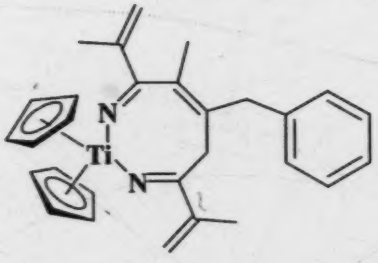
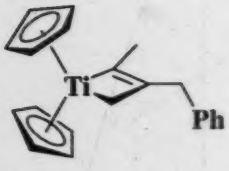
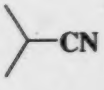
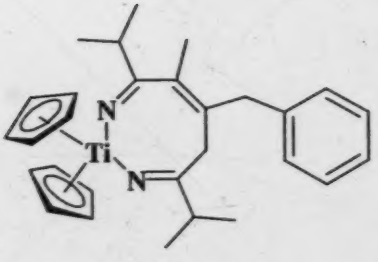
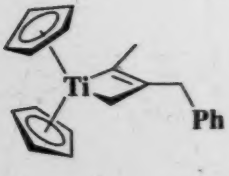
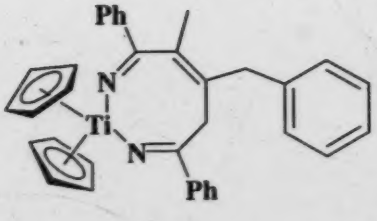


eq. 3.12

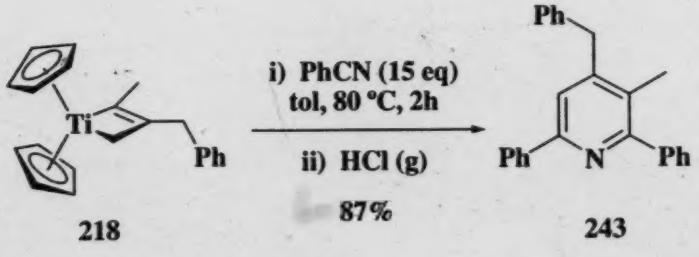
Table 3.2 Selected NMR data for compound **240**

Position	^{1}H NMR data (ppm)	^{13}C NMR data (ppm)
3	–	168.2
6	3.30 (d, ^{2}J = 11.5 Hz, 1H, H6); 3.12 (d, ^{2}J = 11.5 Hz, 1H, H6')	37.4
7	–	160.5
9	3.56 (d, ^{2}J = 15.5 Hz, 1H, H9); 3.24 (d, ^{2}J = 15.5 Hz, 1H, H9')	39.3
10	–	140.52
14	–	143.9
15	5.22 (m, 1H, H15); 5.11 (m, 1H, H15')	114.3
16	1.86 (s, 3H)	20.1
17	–	145.0
18	5.27 (m, 1H, H18); 5.13 (m, 1H, H18')	114.0
19	1.80 (s, 3H)	20.6
20	1.82 (s, 3H)	17.9

Table 3.3 Nitrile double insertion products

starting complex	nitrile	insertion product	yield (%)
 **215**	PhCN	 **233**	97
 **218**		 **240**	99
 **218**		 **241**	86
 **218**	PhCN	 **242**	77

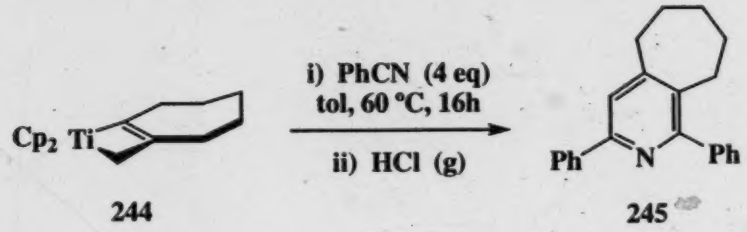
c. Pyridine formation. Tetra-substituted pyridines are formed by direct treatment of the double insertion product with anhydrous HCl, with or without the prior isolation of the double insertion products. To increase the solubility of HCl in toluene, the solution is first cooled to –78 °C. Anhydrous HCl gas is introduced for approximately ten seconds and, upon warming to room temperature, the bis(cyclopentadienyl)titanium(IV) dichloride is formed along with the organic pyridine. A typical example is the synthesis of 4–benzyl–3–methyl–2,6–diphenylpyridine **243** (eq. **3.13**): 1,1–bis(cyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene **218** was treated with excess benzonitrile and heated. The solution was cooled, anhydrous hydrogen chloride gas was introduced, and the reaction mixture allowed to warm to room temperature. Following chromatography on neutral alumina, 4–benzyl–3–methyl–2,6–diphenylpyridine **243**[193] was isolated in 87% as a light yellow oil.



218 **243** eq. 3.13

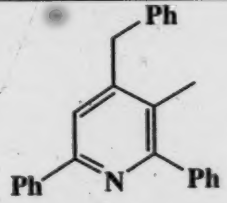
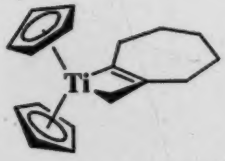
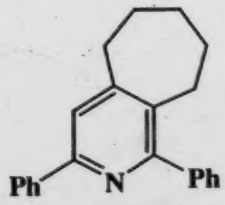
Combining medium–ring synthesis by intramolecular radical alkylation with the pyridine formation protocol offers an efficient method to synthesize substituted bicyclic pyridines. Thus, bicyclic titanacyclobutene 8,8–bis(cyclopentadienyl)titanabicyclo-

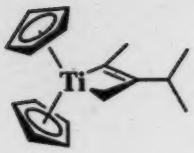
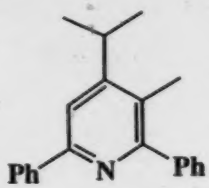
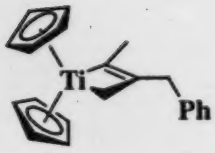
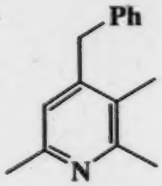
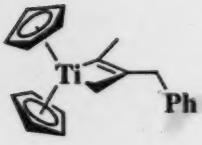
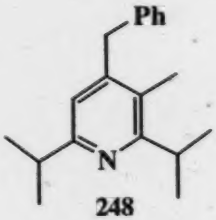
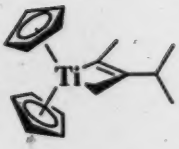
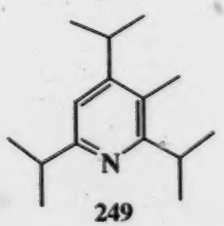
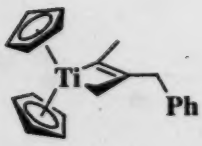
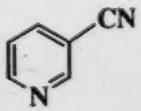
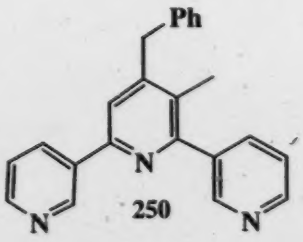
[5.2.0]non–1–(7)–ene **244**,[28] upon treatment with four equivalents of benzonitrile followed by acidolysis with hydrogen chloride gas and column chromatography on neutral alumina, produces 1,3–diphenyl–6,7,8,9–tetrahydro–5H–cyclohepta[c]pyridine **245** as a yellow oil in 81% yield (eq. **3.14**). A range of other pyridines can be constructed from bis(cyclopentadienyl)titanacyclobutene complexes by this method, as recorded in Table **3.4**, and detailed in the experimental section.



244 **245** eq. 3.14

Table **3.4** Tetra-substituted pyridines *via* titanacyclobutene complexes

starting material	nitrile	pyridine	yield (%)
	PhCN	 **243**	87
	PhCN	 **245**	81

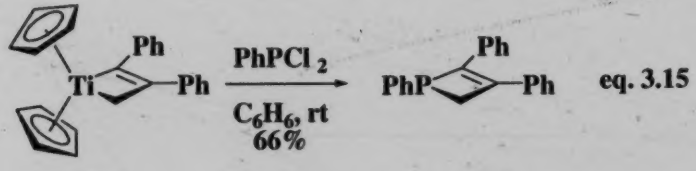
starting material	nitrile	pyridine	yield (%)
	PhCN	 246	70
	MeCN	 247	51
	^{i}PrCN	 248	53
	^{i}PrCN	 249	20
		 250	48

Conditions: *a*: 15 eq. nitrile, 80 °C, 2h; *b*: 4 eq. nitrile, 60 °C, 16h; c: 15 eq. nitrile, 80 °C, 2h; *d*: 15 eq. nitrile, 80 °C, 3h; *e*: 15 eq. nitrile, 80 °C, 2h; *f*: 15 eq. nitrile, 80 °C, 6h; *g*: 12 eq. nitrile, 40 °C, 5 days.

B. ***Conversion of Titanacyclobutene complexes to Phosphorous and Boron Heterocyclobutene Complexes***

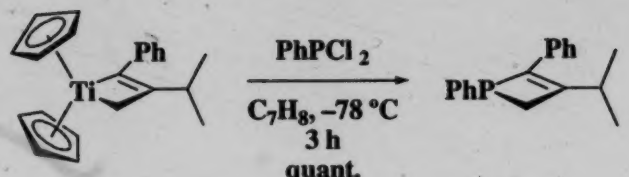
A number of preliminary transmetallation reactions of titanacyclobutene complexes were attempted to find general, robust methods for demetallation reactions that either maintain or increase the degree of functionality in the molecule. Under various solvent and temperature regimes, none of the electrophiles $(Ph_3P)_3PdCl_2$, $Ph(^tBu)SiCl_2$, or Ph_2SiCl_2 provide clean transmetallation products. However, reactions with dichlorophenylphosphine and dichlorophenylborane produce the corresponding heterocyclobutene compounds.

Phosphacyclobutenes are an interesting class of molecules that have only recently been isolated.[182,183] Titanacyclobutene complexes have been shown to react with one equivalent of dichlorophosphine to afford phosphacyclobutene,[182] or two equivalents to afford 1,2–diphosphacyclopentene.[184] Doxsee, for example, reports that 2,3–diphenyl–titanacyclobutene **251** reacts with one equivalent of dichlorophenylphosphine in benzene at room temperature to afford 2,3–diphenylphosphacyclobutene **252** in 66% yield (eq. **3.15**).[183] However, in our hands, treatment of 3–isopropyl–2–phenyltitanacyclobutene **219** in benzene with one equivalent of dichlorophenylphosphine at room temperature



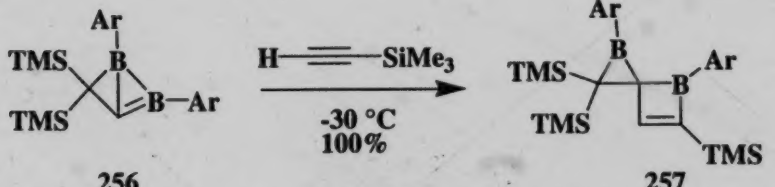
251 **252** eq. 3.15

provides an approximately 1:1 mixture of phosphacyclobutene and 1,2–diphosphacyclopentadiene (by ^{1}H NMR spectroscopy). When the titanacyclobutene is cooled to –35 °C before the phenyldichlorophosphine is added and the reaction mixture maintained at –35 °C, the product mixture consists mainly of the phosphacyclobutene, with only a minor amount of 1,2–diphosphcyclopentadiene. However, when the reaction is run at –78 °C, clean conversion exclusively to 3–isopropyl–2–phenylphosphacyclobutene **255** is observed (eq. **3.16**). Due to the high atmospheric sensitivity of the product as well as the high lipophilicity, purification is practically limited to recrystallization. Unfortunately, complete separation of the reaction by–product bis(cyclopentadienyl)titanium(IV) dichloride is not obtained upon recrystallization, hence a pure sample of **255** was unobtainable. The yield of the reaction therefore cannot be precisely determined, but the reaction appears to be quantitative by NMR spectroscopy. The residual bis(cyclopentadienyl)titanium(IV) dichloride does not hamper spectroscopic identification of the product. The ^{1}H NMR spectrum of **255** at 360 MHz (C_6D_6) reveals the methylene hydrogens as stereochemically inequivalent, each giving rise to a doublet of doublets, one at δ 2.53 and the other at δ 1.86 ($^2J_{HH}$ = 15.0 Hz, $^2J_{HP}$ = 9.4 Hz, 4.2 Hz). The methyl groups of the isopropyl group are also inequivalent, appearing as two doublets at δ 0.96 and δ 0.82 ($^3J_{HH}$ = 6.8 Hz). ^{31}P {^{1}H} NMR spectroscopy (81 MHz, C_6D_6) shows a single resonance at δ –14.82, consistent with known phosphacyclobutene compounds.[29, 182]



219 255 eq. 3.16

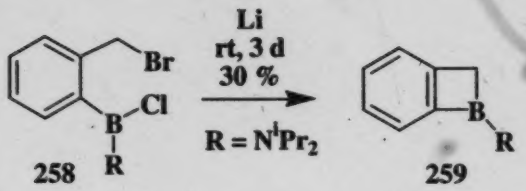
Boracyclobutene complexes are an interesting class of small heterocycles for which no general synthetic route yet exists.[194] One method by which more complex members of this structural class can be accessed is through the reaction of borenes and alkyne. For example, Berndt demonstrated that methyleneborane **256** and trimethylsilylacetylene react at –30 °C to afford 1,4–diboraspiro[2,3]hex–5–ene **257** quantitatively (eq. **3.17**).[195] Alternatively, dihyrobenzoborete **259** can be synthesized by the lithium–mediated 1,4–cyclization of [2–(bromomethyl)phenyl]borane **258** (eq. **3.18**).[196] This process however is non–general: for cases where R ≠ bisisopropylamine no cyclization occurs, and even for the single successful case, the yield is poor.



256 257 eq. 3.17

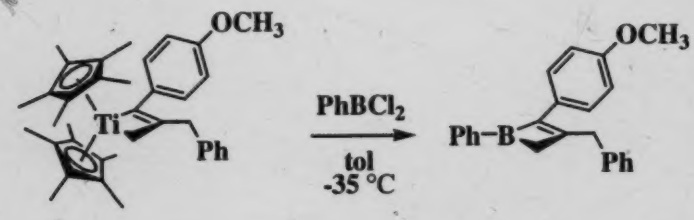
Ar = 2,3,5,6-tetramethylphenyl

Boracyclobutene complexes can also be obtained by the transfer of the organic fraction (exclusive of the ancillary ligand set) of a titanacyclobutene complex to dichlorophenyl boron. Qiu and Stryker successfully demonstrated this transformation



258 259 eq. 3.18

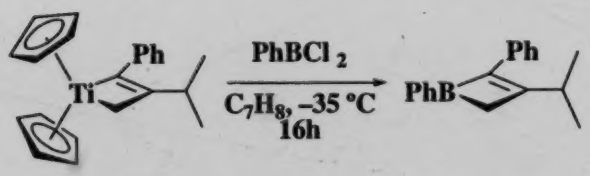
using 1,1–bis(pentamethylcyclopentadienyl)–3–benzyl–2–(4–methoxyphenyl)titanacyclobutene **260** to form 3–benzyl–2–(4–methoxyphenyl)–1–phenylboracyclotene **261** (eq. **3.19**), but were unable to separate the bis(pentamethylcyclopentadienyl)titanium dichloride byproduct from the boracycle product.[29] The different solubility of bis(cyclopentadienyl)titanium dichloride may allow for its separation from the boracyclobutene product, consequently the use of a titanacyclobutene complex from the cyclopentadienyl series was evaluated as a substrate for this reaction. Thus, a toluene solution of **219** at –35 °C was treated with one equivalent of dichlorophenylborane leading, after repeated recrystallizations with cold hexane, to boracyclobutene **262**



260 261 eq. 3.19

(eq. **3.20**) in high yield. Unfortunately, the solubility characteristics of bis(cyclopentadienyl)titanium(IV) dichloride and the boracyclobutene again precluded complete separation, and like the above phosphacyclobutene, 3–isopropyl–1,2–

diphenylboracyclobutene **262** was characterized spectroscopically in the presence of a small amount of residual bis(cyclopentadienyl)titanium(IV) dichloride. Unlike the chiral phosphacyclobutene, however, the methylene hydrogens in boracycle **262** appear as a broad singlet at δ 2.57 in the ^{1}H NMR spectrum, and the isopropyl methyl groups appear as one doublet at δ 1.05 ($^{3}J_{HH}$ = 6.8 Hz, 600 MHz, C_6D_6). The ^{11}B resonance (64 MHz, C_6D_6) appears at δ 69.96, in accord with published values of boracyclobutene complexes.[29, 195, 196]



219 **262** eq. 3.20

C. *Conclusions.*

Nitrile insertion was found to occur in titanacyclobutene complexes derived from the *tert*–butylcyclopentadienyl and cyclopentadienyl ligand series, but not from the pentamethylcyclopentadienyl series. Only two modes of insertion are observed: i) single insertion into the metal-alkyl bond, or ii) double insertion, occuring formally into both the metal–alkyl and metal–vinyl bonds. Single insertion into the metal–vinyl bond is not observed. Exclusively single nitrile insertion was observed for the *tert*–butylcyclopentadienyl series. Confirming Doxsee's earlier observations, either single or

double nitrile insertion into bis(cyclopentadienyl)titanacyclobutene complexes was observed, dependent on the α–substituent of the titanacyclobutene complex.[185] With an α–methyl substituent, double–insertion products were formed, but with an α–phenyl substituent, only single insertion products were generally observed. Pyridines could be accessed, without prior isolation of the double insertion product, directly from the titanacyclobutene complex. As first demonstrated by Doxsee, the double insertion products do not arise from the incorporation of a nitrile into an isolable metal–alkyl bond single insertion product.[185] Instead, they likely arise from insertion into a fleeting metal–vinyl bond insertion product. By the nature of the insertion reaction, pyridines synthesized in this manner possess equivalent α and α' substituents. A method to control the double insertion reaction to allow for mixed double insertion products and therefore tetra–substituted pyridines with four unique substituents would greatly enhance the utility of this process.

Chapter 4. *Experimental Details.*

A. *General*

All air–sensitive manipulations were conducted under a nitrogen atmosphere using standard Schlenk or drybox techniques in a nitrogen atmosphere drybox equipped with a freezer maintained at –35 °C. Unless otherwise stated, all reactions were carried out under a nitrogen atmosphere. The high vacuum line (10^{-5} mm Hg) was used to add solvent and volatile reagents to reaction mixtures at –198 °C via vacuum transfer and to remove volatile compounds from reaction mixtures. Infrared (IR) spectra were recorded on Nicolet 7199 Fourier transform spectrophotometers, and are reported in reciprocal wave numbers (cm^{-1}) calibrated to the 1601 cm^{-1} absorption of polystyrene. All infrared determinations were done on compounds applied as a thin film on KBr or KCl plates and are referred to as "casts."

Nuclear magnetic resonance spectra (NMR) (^1H and ^{13}C) were recorded on Varian INOVA 300, Varian INOVA 600, Varian UNITY 500, Varian UNITY 300, Bruker AM–400, Bruker AM–360, Bruker AM–300, and Bruker AM–200 spectrometers. Chemical shifts are reported in parts per million (ppm, δ) relative to TMS (^1H and ^{13}C), H_3PO_4 (^{31}P) and $BF_3{\bullet}OEt_2$ (^{11}B). Coupling constants are reported in Hertz (Hz). Coupling constants reported as J refer to J_{HH} for ^1H NMR spectra, and J_{CH} for ^{13}C NMR spectra, or could not be unambiguously assigned due to the presence of multiple spin active atoms in close proximity. Coupling constants are reported to 0.1 Hertz, which is

within the limits of instrumental precision, but these values are normally accurate only to within ± 0.5 Hertz. Unless stated otherwise, NMR spectra were obtained at room temperature, approximately 23 °C. Multiplicities are reported as observed. Two–dimensional NMR abbreviations used are: HMQC (heteronuclear multiple quantum correlation), HMBC (heteronuclear multiple bond correlation), HSQC (heteronuclear single quantum correlation), COSY (correlated spectroscopy), APT (attached proton test). HMQC and HMBC experiments are recorded at the ^{1}H frequency. Abbreviations used in the assignment of metallacyclobutene resonances are "α" (positions adjancent to the metal) and "β" (positions distal to the metal).

High resolution mass spectra (HRMS) were obtained on a Kratos MS–80RFA spectrometer operating at 40 eV.

Analytical thin layer chromatography (TLC) was performed on precoated glassbacked silica gel plates, (E. Merck 60 F_{254}, 0.25 mm) and visualized by irradiation with UV light, 14% ethanolic phosphomolybdic acid and heat, aqueous $KMnO_4$–NaOH–K_2CO_3, or iodine supported on silica gel. Flash column chromatographic separations were performed using silica gel 60 (0.040–0.063 mm, E. Merck), or neutral alumina (Fisher). Celite filtrations were performed using a plug of Hyflo Super Cel (Fisher) over glass wool in pipets or alone on cintered glass funnels under vacuum. Cylindrical medium–walled Pyrex vessels equipped with Kontes K–826510 Teflon vacuum stopcocks are referred to as glass bombs.

The following complexes were prepared according to published procedures: C_5Me_5H,[197] bis(pentamethylcyclopentadienyl)titanium(III) chloride,[198,199] bis(*tert*–butylcyclopentadienyl)titanium(III) chloride,[200,201,199] bis(cyclopentadienyl)titanium(III) chloride dimer.[202]

Materials: Unless otherwise indicated, solvents and reagents were purchased from commercial vendors, distilled or passed down a plug of neutral alumina, and degassed prior to used by repeated freeze–pump–thaw cycles on a vacuum line. Benzene, hexanes, pentane, tetrahydrofuran, and diethyl ether were purified by distillation from sodium or potassium benzophenone ketyl. Dichloromethane was distilled from calcium hydride and deoxygenated prior to use.

B. *Experimental Procedures*

i) Intermolecular free radical addition reactions

Methyl 6–bromo–6–deoxy–D–glucopyranoside[134] 123.

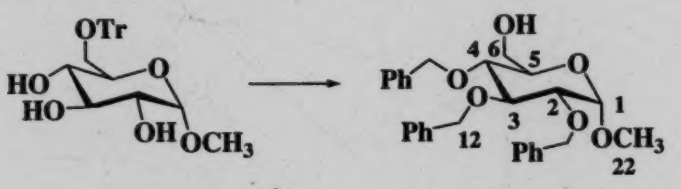
To a solution of methyl–α–D–glucopyranoside (1.00 g, 5.14 mmol) in pyridine was added triphenyl phosphine (1.89 g, 7.21 mmol) and carbon tetrabromide (1.88 g, 5.66 mmol). The solution was heated to 60 °C for 6 hours. The solution was cooled and the solvents removed *in vacuo*. The crude residue was purified by silica gel column chromatography (eluent: hexane/EtOAc, 1:1). The resulting residue was recrystallized from boiling acetone to afford an analytically pure sample of glucopyranoside **123** (0.65 g, 48% yield) as a white waxy solid. Spectroscopic data for methyl 6–bromo–6–deoxy–D–glucopyranoside **123**: **^{1}H NMR** (500 MHz, $CDCl_3$, assignments confirmed by HMQC spectrum) δ 4.64 (d, $^3J_{HH}$ = 3.8 Hz, 1H, H1); δ 3.73 (dd, $^2J_{HH}$ =10.9 Hz, $^3J_{HH}$ = 2.0 Hz, 1H, H6); δ 3.64 (ddd, $^3J_{HH}$ = 6.8 Hz, $^2J_{HH}$ = 1.4 Hz,1H, H5); δ 3.58 (t, $^3J_{HH}$ = 9.2 Hz, 1H, H3); δ 3.51 (dd, $^2J_{HH}$ = 10.9 Hz, $^3J_{HH}$ = 6.8 Hz, 1H, H6'); δ 3.41 (s, 3H, H7); δ 3.37 (dd, $^3J_{HH}$ = 9.8 Hz, $^3J_{HH}$ = 3.8 Hz, 1H, H2); δ 3.21 (t, $^3J_{HH}$ = 9.2 Hz, H4). **^{13}C APT NMR** (125 MHz, CD_3OD, assignments confirmed by HMQC spectrum) δ 101.28 (C1); 74.86 (C3); 73.89 (C4); 73.48 (C2); 72.46 (C5); 55.65 (C7); 34.20 (C6). **HMQC** (500 MHz, decoupled, CD_3OD, selected data only) δ 4.64 (H1) ↔ δ 101.28 (C1); δ 3.73 (H6) ↔ δ 34.20 (C6); δ 3.64 (H5) ↔ δ 72.46 (C5); δ 3.58 (H3) ↔ δ 74.86 (C3); δ 3.51 (H6') ↔ δ 34.20 (C6); δ 3.41 (H7)↔ δ 55.65 (C7); δ 3.37 (H2)↔ δ 73.48 (C2); δ 3.21 (H4) ↔ δ 73.89 (C4). **Anal.** Calcd. for $C_7H_{13}O_5Br$: %C, 32.70, %H, 5.10; Found: %C, 33.1320, %H, 5.0975.

Methyl 6–triphenylmethyl–D–glucopyranoside[203] 124.

124

To a solution of methyl–α–D–glucopyranoside (2.50 g, 12.8 mmol) in pyridine was added chlorortriphenylmethane (3.59 g, 12.8 mmol) and a catalytic amount of DMAP (~10 mg). The solution was stirred at room temperature for 16 hours. The solvents were removed *in vacuo*. The crude residue was purified by silica gel column chromatography (hexane:EtOAc, 1:1), to afford triphenylmethyl protected glucopyranoside **124** (5.22 g, 93% yield) as a white solid.[203] Spectroscopic data for methyl 6–triphenylmethyl–D–glucopyranoside **124**: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 8.65 (d, J = 4.5 Hz, 2H); δ 7.82 (tt, J = 7.7 Hz, J = 1.8 Hz, 1H); δ 7.47–7.39 (m, 6H); δ 7.33–7.29 (m, 6H); δ 7.26–7.24 (m, 2H); δ 4.78 (d, J = 3.9 Hz, 1H); δ 3.66 (d, J = 9.4 Hz, 1H); δ 3.54 (d, J = 9.4 Hz, 1H); δ 3.54 (m, 1H); δ 3.43 (s, 3H); δ 3.40 (m, 3H).

Methyl 2,3,4–tris–O–benzyl–6–hydroxy–D–glucopyranoside[204] 125.

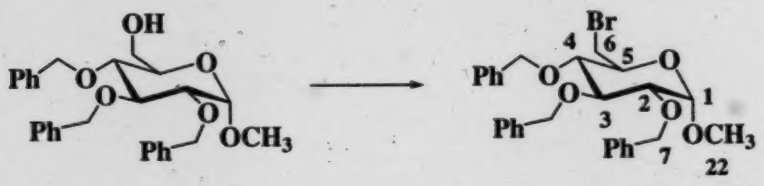


125

To a solution of methyl 6–triphenylmethyl–D–glucopyranoside **124** (5.00 g, 11.45 mmol) in dry DMF at 0 °C was added sodium hydride (60% dispersion in mineral oil, 1.65 g, 41.00 mmol). The solution was stirred at 0 °C for 4 hours, then benzyl bromide (7 g, 41.00 mmol) was added slowly and the solution was allowed to warm to room temperature. The solution was stirred under nitrogen at room temperature for 36 hours, after which only one spot was visible by tlc. The reaction mixture containing crude methyl 2,3,4–tris–O–benzyl–6–triphenylmethyl–D–glucopyranoside was extracted into ether, reduced by rotary evaporation, and then dissolved in methanol. Approximately one millilitre of trifluoroacetic acid was added, and the solution was heated to reflux for approximately 24 hours. After silica gel chromatography, methyl 2,3,4–tris–O–benzyl–6–hydroxy–D–glucopyranoside, was isolated as a white solid (5.17 g, 64% yield). Spectroscopic data for **125**: **^{1}H NMR** (500 MHz, $CDCl_3$, assignments confirmed by HMQC and HMBC spectra) δ 7.4–7.25 (m, 15H, ArH); 5.00 (d, $^2J_{HH}$ = 10.9 Hz, 1H, $-CH_2-$Ph); 4.89 (d, $^2J_{HH}$ = 11.2 Hz, 1H, $-CH_2-$Ph); 4.84 (d, $^2J_{HH}$ = 10.9 Hz, 1H, $-CH_2-$Ph); 4.80 (d, $^2J_{HH}$ = 12.1 Hz, 1H, $-CH_2-$Ph); 4.66 (d, $^2J_{HH}$ = 12.1 Hz, 1H, $-CH_2-$Ph); 4.65 (d, $^2J_{HH}$ = 11.2 Hz, 1H, $-CH_2-$Ph); 4.57 (d, $^3J_{HH}$ = 3.4 Hz, 1H, H1); 4.01 (dd, $^3J_{HH}$ = 9.2

Hz, 1H, H3); 3.78–3.63 (m, 3H, H5, H6, H6'); 3.53 (dd, $^3J_{HH}$ = 9.2 Hz, 1H, H4), 3.51 (dd, $^3J_{HH}$ = 9.2 Hz, $^3J_{HH}$ = 3.4 Hz, 1H, H2); 3.38 (s, 3H, H22); 1.82 (br s, 1H, –OH). **^{13}C APT NMR** (125 MHz, CDCl3, assignments confirmed by HMQC and HMBC spectra) δ 138.72 (–CH_2–Ph ipso); 138.13 (–CH_2–Ph ipso); 138.09 (–CH_2–Ph ipso); 128.42 (Ar); 128.35 (Ar); 128.06 (Ar); 127.96 (Ar); 127.91 (Ar); 127.89 (Ar); 127.80 (Ar); 127.56 (Ar); 98.12 (C1); 81.91 (C3); 79.95 (C2); 77.39 (C4); 75.68 (C12); 74.97 (–CH_2–Ph); 73.35 (–$\underline{C}H_2$–Ph); 70.68 (C5); 61.75 (C6); 55.12 (C22). **HMQC** (500 MHz, decoupled, $CDCl_3$, selected data only) δ 5.00, δ 4.84 (–$C\underline{H}_2$–Ph) ↔ δ 75.68 (–CH_2–$\underline{Ph}$); δ 4.89, 4.65 (–$C\underline{H}_2$–Ph) ↔ δ 74.97 (–CH_2–$\underline{Ph}$); δ 4.80, 4.66 (–$C\underline{H}_2$–Ph) ↔ δ 73.35 (–CH_2–$\underline{Ph}$); δ 4.57 (H2) ↔ δ 98.12 (C2); δ 4.01 (H4)↔ δ 81.91 (C4); δ 3.74 (H11) ↔ δ 61.75 (C11); δ 3.65 (H6) ↔ δ 70.68 (C6); δ 3.53 (H5) ↔ δ 77.39 (C5); δ 3.51 (H3) ↔ δ 79.95 (C3); δ 3.38 (H10)↔ δ 55.12 (C10). **HMBC** (300 MHz, $CDCl_3$, selected data only) δ 4.57 (H2) ↔ δ 81.91 (C4), 70.68 (C6), 55.12 (C10); δ 4.01 (H4) ↔ δ 79.95 (C3), 77.39 (C5); 75.68 (–CH_2–$\underline{Ph}$ of C4); δ 3.38 (H10) ↔ δ 98.12 (C2). **HRMS** $C_{28}H_{31}O_6$ requires 463.21124, found 463.21207. **Anal.** Calcd for $C_{28}H_{32}O_6$: C, 72.39, H, 6.94; Found: C, 72.2536, H, 7.0104.

Methyl 2,3,4–tris–O–benzyl–6–bromo–6–deoxy–D–glucopyranoside[136] 126.



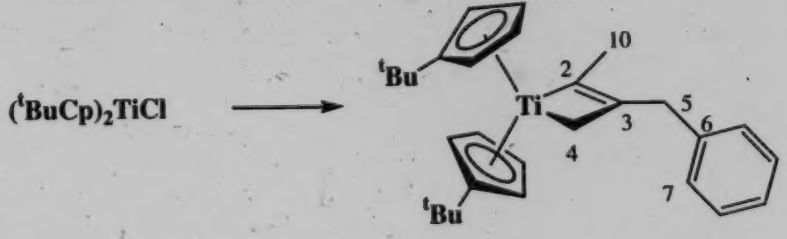
125 **126**

To a solution of methyl 2,3,4–tris–O–benzyl–6–hydroxy–D–glucopyranoside **125** (1.20 g, 2.58 mmol) in pyridine was added triphenyl phosphine (0.94 g, 3.61 mmol) and carbon tetrabromide (0.94 g, 2.84 mmol). The solution was heated to 60 °C for 6 hours, after which the solution was cooled to room temperature then the solvent removed *in vacuo*. The crude material was separated by silica gel column chromatography (eluent: hexane), to afford **126** (0.92 g, 68% yield) as a white waxy solid.[136] Approximately 20% of the starting material was recovered. Spectroscopic data for methyl 2,3,4–tris–O–benzyl–6–bromo–6–deoxy–D–glucopyranoside **126**: **^{1}H NMR** (300 MHz, $CDCl_3$, assignments confirmed by GCOSY spectrum) δ 7.4–7.25 (m, 15H, ArH); 5.01 (d, $^2J_{HH}$ = 10.9 Hz, 1H, –CH$_2$–Ph); 4.94 (d, $^2J_{HH}$ = 10.9 Hz, 1H, –CH$_2$–Ph); 4.82 (d, $^2J_{HH}$ = 10.8 Hz, 1H, –CH$_2$–Ph); 4.81 (d, $^2J_{HH}$ = 12.1 Hz, 1H, –CH$_2$–Ph); 4.67 (d, $^2J_{HH}$ = 10.8 Hz, 1H, –CH$_2$–Ph); 4.66 (d, $^2J_{HH}$ = 12.1 Hz, 1H, –CH$_2$–Ph); 4.63 (d, $^3J_{HH}$ = 3.6 Hz, 1H, H1); 4.01 (dd, $^3J_{HH}$ = 9.3 Hz, $^3J_{HH}$ = 9.2 Hz, 1H, H3); 3.80 (ddd, $^3J_{HH}$ = 9.6 Hz, $^3J_{HH}$ = 5.2 Hz, $^3J_{HH}$ = 2.5 Hz, 1H, H5); 3.64 (dd, $^2J_{HH}$ = 11.0 Hz, $^3J_{HH}$ = 2.5 Hz, 1H, H6); 3.56 (dd, $^2J_{HH}$ = 11.0 Hz, $^3J_{HH}$ = 2.5 Hz, 1H, H6'), 3.55 (dd, $^3J_{HH}$ = 9.3 Hz, $^3J_{HH}$ = 3.6 Hz, 1H, H2); 3.50 (dd, $^3J_{HH}$ = 9.4 Hz, $^3J_{HH}$ = 9.4 Hz, 1H, H4); 3.38 (s, 3H, H22). **^{1}H GCOSY NMR** (300 MHz, $CDCl_3$,

selected data only) δ 4.63 (H1) ↔ δ 3.55 (H2); δ 4.01 (H3) ↔ δ 3.55, 3.50 (H2, 4); δ 3.80 (H5) ↔ δ 3.56, 3.50 (H6, 6', 4). **^{13}C APT** (75 MHz, $CDCl_3$, assignments confirmed by HMQC spectrum) δ 138.62 (–CH_2–Ph *ipso*); 138.07 (–CH_2–Ph *ipso*); 138.04 (–CH_2–Ph *ipso*); 128.54 (–CH_2–Ph); 128.47 (–CH_2–Ph); 128.14 (–CH_2–Ph); 128.01 (–CH_2–Ph); 127.97 (–CH_2–Ph); 127.72 (–CH_2–Ph); 98.19 (C1); 81.81 (C3); 80.03 (C2); 79.64 (C4); 75.81 (–CH_2–Ph); 75.32 (–CH_2–Ph); 73.49 (–CH_2–Ph); 69.41 (C5); 55.42 (C22); 33.69 (C6). **HMQC** (300 MHz, decoupled, $CDCl_3$, selected data only) δ 5.01 (–CH_2–Ph) ↔ δ 75.81 (–CH_2–Ph); δ 4.94 (–CH_2–Ph) ↔ δ 75.32 (–CH_2–Ph); δ 4.82 (–CH_2–Ph) ↔ δ 75.81 (–CH_2–Ph); δ 4.81 (–CH_2–Ph) ↔ δ 73.49 (–CH_2–Ph); δ 4.67 (–CH_2–Ph) ↔ δ 75.32 (–CH_2–Ph); δ 4.66 (–CH_2–Ph) ↔ δ 73.49 (–CH_2–Ph); δ 4.63 (H1)↔ δ 98.19 (C1); δ 4.01 (H3)↔ δ 81.81 (C3); δ 3.80 (H5)↔ δ 69.41 (C5); δ 3.64 (H6) ↔ δ 33.69 (C6); δ 3.56 (H6') ↔ δ 33.69 (C6); δ 3.55 (H2) ↔ δ 80.03 (C2); δ 3.50 (H4) ↔ δ 79.64 (C4); δ 3.38 (H22) ↔ δ 55.42 (C22). **Anal.** Calcd. for $C_{28}H_{31}O_5Br$: C, 63.76, H, 5.92. Found C, 63.4562, H, 5.9030.

ii) Intermolecular vinyl radical addition reactions

1,1–Bis(*tert*–butylcyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene 109.

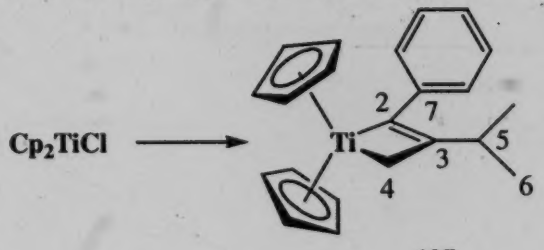


109

To a cold (–35 °C) solution of (^{t}BuCp)$_2$TiCl (10 mg, 0.030 mmol) and SmI_2 (0.1 M in THF, 0.92 mL, 0.0916 mmol) in dry THF (~1 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–35 °C) solution of 2–butynyl bromide (4.1 mg, 0.0305 mmol). The solution was allowed to sit at –35 °C for one minute, then benzyl bromide (5.2 mg, 0.0305 mmol) was added and the solution allowed to warm to room temperature and sit for two hours during which time the solution colour changed from turquoise to dark red. The solvent was evaporated *in vacuo* and the residue was triturated with pentane. The extract was filtered through a short column of celite followed by concentration to give a spectroscopically clean dark red solid which was not further purified (13 mg, 99%). Spectroscopic data for **109**: **^{1}H NMR** (360 MHz, C_6D_6) δ 7.21 (m, 2H, Ar<u>H</u>); 7.15 (m, 1H, obscured by residual C_6H_6, Ar<u>H</u>); 7.09 (m, 2H, H7); 5.79 (dd, $^3J_{HH}$ = 5.3 Hz, $^4J_{HH}$ = 2.8 Hz, 2H, ^{t}BuCp<u>H</u>); 5.52 (dd, $^3J_{HH}$ = 5.3 Hz, $^4J_{HH}$ = 2.8 Hz, 2H, ^{t}BuCp<u>H</u>); 5.34 (dd, $^3J_{HH}$ = 4.9 Hz, $^4J_{HH}$ = 2.5 Hz, 2H, ^{t}BuCp<u>H</u>); 5.27 (dd, $^3J_{HH}$ = 4.9 Hz, $^4J_{HH}$ = 2.5 Hz, 2H, ^{t}BuCp<u>H</u>); 3.30 (s, 2H, H5), 3.03 (q, $^5J_{HH}$ = 1.9 Hz, 2H, H4); 2.29 (t, $^5J_{HH}$ = 1.9 Hz, 3H, H10); 1.07 (s, 18H, ^{t}<u>BuCp</u>). **^{13}C (APT) NMR** (125 MHz, C_6D_6, assignments confirmed by HMQC and HMBC spectra) δ 207.88 (C2); 141.16 (C6); 139.47 (^{t}BuCp *ipso*); 129.51 (C9); 128.30 (C7); 125.78 (Ar); 110.26 (^{t}BuCp); 109.67 (^{t}BuCp); 109.45 (^{t}BuCp); 107.33 (^{t}BuCp); 95.92 (C3); 72.35 (C4); 35.59 (C5); 32.69 (^{t}<u>BuCp</u>); 31.55 (^{t}<u>BuCp</u>); 22.71 (C10). **HMQC** (300 MHz, decoupled, C_6D_6, selected data only) δ 5.79 (^{t}BuCp <u>H</u>) ↔ δ 110.26 (^{t}BuCp); δ 5.52 (^{t}BuCp <u>H</u>) ↔ δ 109.45 (^{t}BuCp); δ 5.34 (^{t}BuCp <u>H</u>) ↔ δ 107.33 (^{t}BuCp); δ 5.27 (^{t}BuCp <u>H</u>) ↔ δ 109.67 (^{t}BuCp);

δ 3.30 (H5) ↔ δ 35.59 (C5); δ 3.03 (H4) ↔ δ 72.35 (C4); δ 2.29 (H10) ↔ δ 22.71 (C10); δ 1.07 (^{t}BuCp) ↔ δ 31.55 (^{t}BuCp). **HMBC** (300 MHz, decoupled, C_6D_6, selected data only) δ 7.21 (ArH) ↔ δ 141.16 (Ar *ipso*), 128.30 (Ar); δ 7.09 (H7) ↔ δ 129.51 (C9), 35.59 (C5); δ 5.52 (^{t}BuCp H) ↔ δ 139.47 (^{t}BuCp *ipso*); δ 5.34 (^{t}BuCp H) ↔ δ 139.47 (^{t}BuCp *ipso*); δ 3.30 (H5) ↔ δ 207.88 (C2), 141.16 (C6), 128.30 (C7), 95.92 (C3), 72.35 (C4); δ 3.03 ↔ δ 207.88 (C2), 95.92 (C3), 35.59 (C5); δ 2.29 (H10) ↔ δ 207.88 (C2), 95.92 (C3); δ 1.07 (^{t}BuCp) ↔ δ 139.47 (^{t}BuCp *ipso*), 31.55 (^{t}BuCp).

1.1–Bis(cyclopentadienyl)–3–isopropyl–2–phenyltitanacyclobutene 127.

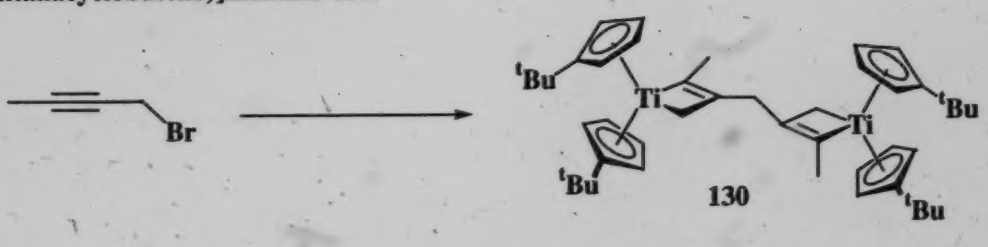


127

To a cold (–35 °C) solution of Cp_2TiCl (405 mg, 1.90 mmol) and SmI_2 (0.1 M in THF, 57 mL, 5.69 mmol) in dry THF (1.2 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–35 °C) solution of 3–bromo–1–phenylpropyne (370 mg, 1.90 mmol) followed immediately by isopropyl iodide (322.0 mg, 1.90 mmol). The solution was allowed to warm to room temperature with stirring over a 16 hour period. During that time the colour changed from turquoise to blood red. Solvent was removed *in vacuo* and the residue triturated with dry pentane, then filtered

through a plug of celite. Recrystallization from pentane yields 1,1–bis(cyclopentadienyl)–3–isopropyl–2–phenyltitanacyclobutene **127** (390 mg, 61% yield) as a spectroscopically clean dark red powder. Spectroscopic data for **127**: **^{1}H NMR** (500 MHz, C_6D_6) δ 7.26 (dddd, $^3J_{HH}$ = 7.0 Hz, $^3J_{HH}$ = 6.0 Hz, $^2J_{HH}$ = 1.5 Hz, $^2J_{HH}$ = 1.0 Hz, 2H, ArH *meta*); 7.02 (tt, $^3J_{HH}$ = 6.0 Hz, $^4J_{HH}$ = 1.0 Hz, 1H, ArH *para*); 6.95 (ddd, $^3J_{HH}$ = 7.0 Hz, $^4J_{HH}$ = 1.5 Hz, $^4J_{HH}$ = 1.0 Hz, 2H, ArH *ortho*); 5.58 (s, 10H, CpH); 3.21 (s, 2H, H4); 2.67 (septet, $^3J_{HH}$ = 5.5 Hz, 1H, H5); 0.91 (d, $^3J_{HH}$ = 5.5 Hz, 6H, H6). **^{13}C {^{1}H} NMR** (125 MHz, C_6D_6, assignments confirmed by HMQC and HMBC spectra) δ 210.15 (C2), 148.89 (C7); 124.84 (Ar *para*); 124.11 (Ar *ortho*); 111.47 (Cp); 99.67 (C3); 69.21 (C4); 27.59 (C5); 21.27 (C6). **HMQC** (500 MHz, decoupled, C_6D_6) δ 6.95 (ArH *ortho*) ↔ δ 124.11 (Ar *ortho*); δ 3.21 (H4) ↔ δ 69.21 (C4); δ 0.91 (H6) ↔ δ 21.27 (C6). **HMBC** (500 MHz, C_6D_6, selected data only) δ 7.26 (ArH *meta*) ↔ δ 148.89 (Ar *ipso*); δ 7.02 (ArH *para*) ↔ δ 124.84 (Ar *ortho*); δ 6.95 (ArH *ortho*) ↔ δ 210.15 (C2), 124.11 (Ar *para*); δ 3.21 ↔ δ 210.15 (C2), 148.89 (Ar *ipso*), 124.11 (Ar *ortho*), 99.67 (C3), 27.59 (C5). **Anal.** Calcd. for $C_{22}H_{24}Ti$: C, 78.57, H, 7.19. Found: C, 79.2434, H, 7.0687.

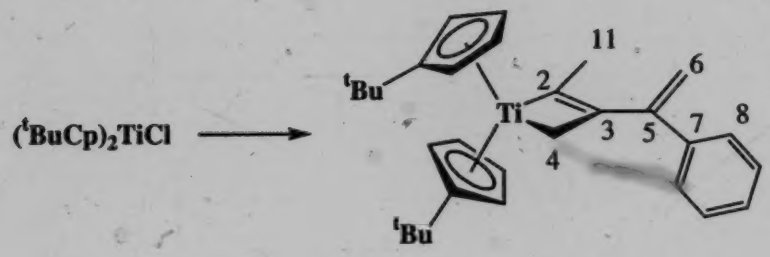
Di–1,1'[3–(1,1–bis(*tert*–butylcyclopentadienyl)–2–methyl–3–titanacyclobuteno)]methane 130.



130

To a cold (–35 °C) solution of (^{t}BuCp)$_2$TiCl (200 mg, 0.61 mmol) and SmI_2 (0.1 M in THF, 15.3 mL, 1.53 mmol) in dry THF (~3 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–35 °C) solution of 2–butynyl bromide (81.6 mg, 0.61 mmol). The solution was allowed to sit at –35 °C for one minute, then diiodomethane (42.6 mg, 0.16 mmol) was added and the solution maintained at –35 °C for 16 hours. After this period, SmI_2 (0.1 M in THF, 3.1 mL, 0.31 mmol) was added at –35 °C, followed by diiodomethane (42.6 mg, 0.16 mmol) and the solution maintained at –35 °C for 16 hours. After this period, the solvent was evaporated *in vacuo* and the residue was triturated with pentane. The extract was filtered through a short column of celite followed by concentration to give a dark red solid (140 mg, 65%). Spectroscopic data for **130**: **^{1}H NMR** (360 MHz, C_6D_6) δ 5.92 (q, J = 2.5 Hz, 4H); δ 5.68 (q, J = 2.5 Hz, 4H); δ 5.52 (q, J = 2.8 Hz, 4H); δ 5.43 (q, J = 2.8 Hz, 4H); δ 3.20 (m, 4H); δ 2.75 (s, 2H); δ 2.35 (s, 6H); δ 1.15 (s, 36H). **^{13}C NMR** (75 MHz, C_6D_6) δ 211.7; δ 139.5; δ 110.1; δ 109.5; δ 109.1; δ 107.4; δ 94.9; δ 76.0; δ 32.7; δ 31.7; δ 29.0; δ 23.1. **HMQC** (600 MHz, decoupled, C_6D_6, selected data only) δ 5.92 (^{t}BuCp H) ↔ δ 110.1 (^{t}BuCp); δ 5.68 (^{t}BuCp H) ↔ δ 109.1 (^{t}BuCp); δ 5.52 (^{t}BuCp H) ↔ δ 109.5 (^{t}BuCp); δ 5.43 (^{t}BuCp H) ↔ δ 107.4 (^{t}BuCp); δ 3.20 ↔ δ 76.0; δ 2.75 ↔ δ 29.0; δ 2.35 ↔ δ 23.1; δ 1.15 ↔ δ 31.7.

1,1–Bis(tert–butylcyclopentadienyl)–3–(1–phenylethene)–2–methyltitanacyclobutene 140.



140

To a cold (–35 °C) solution of (^{t}BuCp)$_2$TiCl (20 mg, 0.061 mmol) and SmI_2 (0.1 M in THF, 1.2 mL, 0.122 mmol) in dry THF (1.2 mL) was added a cold (–35 °C) solution of 2–butynyl bromide (8.2 mg, 0.061 mmol). The solution was allowed to warm to room temperature with stirring over a 15 minute period. During that time the colour changed from turquoise to brown. After 15 minutes, 6 mL of dry benzene was added, followed by SmI_2 (0.1 M in THF, 0.61 mL) and HMPA (132 mg, 0.737 mmol) at room temperature. Upon addition of the HMPA, the solution turned purple. β–bromostyrene (11 mg, 0.061 mmol) was added and the mixture heated at 60 °C for 1 h during which time the colour of the solution turned blood red. After cooling to room temperature, the solvent was evaporated *in vacuo* and the residue was triturated with pentane. The extract was filtered through a short column of celite followed by concentration to give a spectroscopically clean red solid (25.8 mg, 95%). Spectroscopic data for **140**: **^{1}H NMR** (300 MHz, C_6D_6) δ 7.33 (d, J=8.1 Hz, 2 H, C_6H_5); 7.21 (t, J_{obs}=8.1 Hz, 2 H, C_6H_5); 7.1 (obscured by C_6D_6

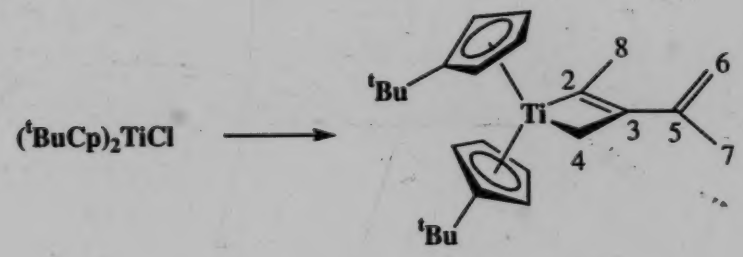
peak, C_6H_5); 5.91 (q, J_{obs}=2.3 Hz, 2H, $^tBuC_5\underline{H}_4$); 5.63 (q, J_{obs}=2.3 Hz, 2H, $^tBuC_5\underline{H}_4$); 5.58 (q, J_{obs}=2.3 Hz, 2H, $^tBuC_5\underline{H}_4$); 5.44 (q, J_{obs}=2.3 Hz, 2H, $^tBuC_5\underline{H}_4$); 5.42 (d, J=2.0 Hz, 1 H, H6); 4.91 (d, J=2.0 Hz, 1 H, H6'); 3.22 (q, J=2.0 Hz, 2 H, H4); 2.22 (t, J= 2.0 Hz, 1 H, H11); 1.08 (m, 18 H, $^t\underline{Bu}C_5H_4$). **^{13}C (APT) NMR** (75 MHz, C_6D_6, assignments confirmed by HMQC and HMBC spectra) δ 212.3 (C2), 147.9 (C5), 142.8 (C7), 139.7 ($^tBuC_5H_4$, ipso), 128.5 (C8), 127.2 (C9), 127.2 (C10), 111.9 (C6), 111.0 ($^tBuC_5H_4$, ring), 110.2 ($^tBuC_5H_4$, ring), 110.0 ($^tBuC_5H_4$, ring), 107.5 ($^tBuC_5H_4$, ring), 99.3 (C3), 72.9 (C4), 32.7 (C15), 31.5 (C16), 23.9 (C11). **HMQC** (300 MHz, decoupled, C_6D_6) δ 7.21 (C_6H_5) ↔ δ 128.5 (C8); δ 7.33 (C_6H_5) ↔ δ 127.2 (C10); δ 5.91 ($^tBuC_5\underline{H}_4$) ↔ δ 111.0 ($^tBuC_5H_4$, ring); 5.58 ($^tBuC_5\underline{H}_4$) ↔ δ 110.2 ($^tBuC_5H_4$, ring); δ 5.63 ($^tBuC_5\underline{H}_4$) ↔ δ 110.0 ($^tBuC_5H_4$, ring); δ 5.44 ($^tBuC_5\underline{H}_4$) ↔ δ 107.5 ($^tBuC_5H_4$, ring); δ 5.42 (H6), 4.92 (H6') ↔ δ 111.9 (C6); δ 3.22 (H4) ↔ δ 72.9 (C4); δ 1.08 ($^t\underline{Bu}C_5H_4$) ↔ δ 31,5 (C16); δ 2.22 (H11) ↔ δ 23.9 (C11). **HMBC** (300 MHz, C_6D_6, selected data only) δ 2.22 (H11) ↔ δ 212.3 (C2), δ 99.3 (C3); δ 3.22 (H4) ↔ δ 212.3 (C2), δ 147.9 (C5), δ 99.3 (C3); δ 5.42 (H6), 4.91 (H6') ↔ δ 147.9 (C5), 142.8 (C7); δ 1.08 ($^t\underline{Bu}C_5H_4$) ↔ δ 139.7 ($^tBuC_5H_4$, ipso), δ 31.5 (C15). **HRMS** for $C_{30}H_{38}Ti$ requires *m/z* 446.24530, found *m/z* 446.24568.

1,1–Bis(tert–butylcyclopentadienyl)–3–(1–phenylethene)–2–methyltitanacyclobutene 140.

Following the same general procedure as the above example, the reaction was carried out using DMPU to form the reductant. Thus, in place of HMPA, DMPU (94 mg, 0.737

mmol) was added to the solution at room temperature. A red solid identical spectroscopically to the product of the above reaction was recovered. (26.6 mg, 98%).

1,1–Bis(*tert*–butylcyclopentadienyl)–3–(isopropenyl)–2–methyltitanacyclobutene 143.



143

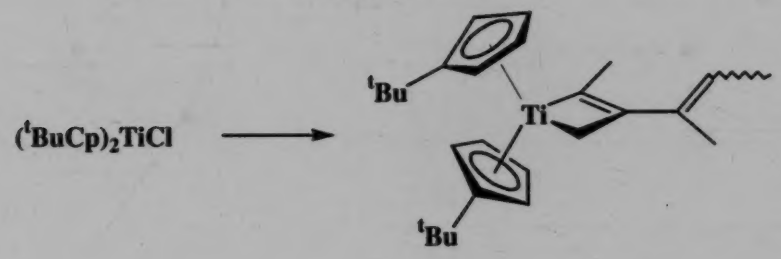
To a cold (–35 °C) solution of (^{t}BuCp)$_2$TiCl (10 mg, 0.0305 mmol) and SmI_2 (0.1 M in THF, 0.92 mL, 0.0916 mmol) in dry THF (~1 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–35 °C) solution of 2–butynyl bromide (4.1 mg, 0.0305 mmol). The solution was allowed to sit at –35 °C for one minute. Cold DMPU (–35 °C, 47.0 mg, 0.3663 mmol) was added and the colour of the solution changed from turquoise to purple. Immediately, 2–bromo–propene (3.7 mg, .030 mmol) was added to the solution and the solution shaken, then allowed to warm to room temperature. During that time the colour changed from turquoise to red. After sitting at room temperature for 10 hours, the solvent was evaporated *in vacuo* and the residue was triturated with pentane. The extract was filtered through a short column of

Celite followed by concentration to give a red oil (12.0 mg, 100%). Spectroscopic data for **143**: **^{1}H NMR** (360 MHz, C_6D_6) δ 5.85 (wide singlet, 2H, ^{t}BuCp); 5.52 (broad singlet, 4H, ^{t}BuCp); 5.39 (broad singlet, 2H, ^{t}BuCp); 5.06 (broad singlet, 1H, H6); 4.72 (broad singlet, 1H, H6'); 3.19 (broad singlet, 2H, H4); 2.30 (broad singlet, 3H, H8); 1.86 (broad singlet, 3H, H7). **^{13}C (APT) NMR** (75 MHz, C_6D_6) δ 211.1 (C2), 142.9 (C5), 139.6 (^{t}BuCp *ipso*), 111.6 (C6); 111.0 (^{t}BuCp); 110.5 (^{t}BuCp); 109.5 (^{t}BuCp); 107.3 (^{t}BuCp); 99.7 (C3); 70.6 (C4); 32.7 (^{t}BuCp); 31.7 (tBuCp); 23.9 (C5); 22.9 (C8). **HRMS** for $C_{25}H_{36}Ti$ requires *m/z* 384.22964, found 384.22944.

1,1–Bis(*tert*–butylcyclopentadienyl)–3–(isopropenyl)–2–methyltitanacyclobutene 143.

Following the same procedure as for the above reaction, titanacyclobutene complex **143** was synthesized using HMPA. Thus, in place of DMPU, HMPA (66 mg, 0.36 mmol) was added to the reaction flask. The product of the reaction was recovered as a red oil which was spectroscopically identical to the product of the above reaction (11.7 mg, 100%)

1,1–Bis(*tert*–butylcyclopentadienyl)–3–(2,3–dimethylethenyl)–2–methyltitana-cyclobutene 146.



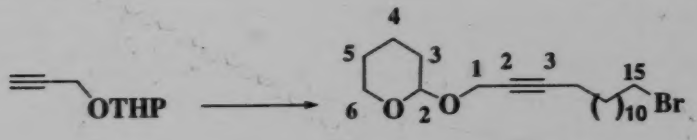
146

To a cold (–35 °C) solution of (^{t}BuCp)$_2$TiCl (10 mg, 0.0305 mmol) and SmI_2 (0.1 M in THF, 0.92 mL, 0.092 mmol) in dry THF (~1 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–35 °C) solution of 2–butynyl bromide (4.1 mg, 0.0305 mmol). The solution was allowed to sit at –35 °C for one minute. Cold DMPU (–35 °C, 47 mg, 0.366 mmol) was added and the colour of the solution changed from turquoise to purple. Immediately, *trans* 2–bromobut–2–ene (4 mg, .030 mmol) was added to the solution and the solution shaken, then maintained at –35 °C for 16 hours after which the solution was warmed to room temperature and allowed to stand for four hours. The solvent was evaporated *in vacuo* and the residue was triturated with pentane. The extract was filtered through a short column of Celite followed by concentration to give a mixture of two products as an impure red oil (8.3 mg, 68%). Spectroscopic data for **146**: signals cannot be attributed definitely to minor/major

product, and are reported as observed: **^{1}H NMR** (360 MHz, C_6D_6) δ 5.90; 5.88; 5.66; 5.58; 5.51; 5.40; 5.35; 3.29; 3.26; 2.64; 2.43; 2.28; 2.17; 1.71; 1.47; 1.46; 1.20; 1.12. **^{13}C NMR** (125 MHz, C_6D_6) δ 211.1; 210.2; 139.5; 139.4; 139.2; 139.2; 134.0; 133.2; 120.1; 119.3; 110.9; 110.3; 110.3; 110.0; 109.9; 109.6; 107.4; 107.3; 100.75; 97.5; 73.5; 72.1; 67.8; 47.6; 32.9; 32.8; 31.7; 23.9; 23.5; 21.9; 16.0; 14.8; 14.2. **HRMS** for $C_{26}H_{38}Ti$ requires *m/z* 398.24530, found 398.24571.

iii) Medium and large ring synthesis *via* intramolecular radical cyclization reactions

2–(15–Bromo–pentadec–2–ynyloxy)–tetrahydropyran 163.



163

Ammonia was condensed into a round bottom flask fitted with an ammonia reflux condenser and rubber septum and was kept under dry nitrogen atmosphere. To approximately 100 mL of liquid ammonia at –78 °C was added 2–(prop–2–ynyloxy)–tetrahydropyran (0.85g, 6.09 mmol). n–BuLi (2.44 mL, 6.09 mmol, 2.5 M) was then added via syringe and the solution stirred and allowed to warm to approximately –50 °C

over one hour. 1,12–dibromododecane (2g, 6.09 mmol) was added to the flask and the solution stirred for approximately five days at –50 °C. The reaction was quenched by allowing the ammonia to boil off, and the gummy reside was partitioned between water and ether. The ether fraction was reduced by rotary evaporation and purified by silica gel column chromatography (eluent: petroleum ether, progressing to 20:1 petroleum ether/ethyl acetate) Product 2–(15–bromo–pentadec–2–ynyloxy)–tetrahydropyran (0.35g, 15% yield) recovered as a white solid **163**. Spectroscopic data for 2–(15–bromo–pentadec–2–ynyloxy)–tetrahydropyran: **^{1}H NMR** (300 MHz, $CDCl_3$, assignments confirmed by HMQC spectrum) δ 4.82 (t, 1H, H2); 4.24 (AB quartet of triplets, $^2J_{HH}$ = 15.2 Hz, $^5J_{HH}$ = 2.3 Hz, 2H, H8); 3.85 (ddd, $^2J_{HH}$ = 11.8 Hz, $^3J_{HH}$ = 8.4 Hz, $^3J_{HH}$ = 3.1 Hz, 1H, H6); 3.53 (m, 1H, H6'); 3.41 (t, $^3J_{HH}$ = 7.0 Hz, 2H, H22); 2.21 (tt, $^3J_{HH}$ = 12.0 Hz, $^5J_{HH}$ = 2.3 Hz, 2H, H11); 1.85 (p, $^3J_{HH}$ = 7.0 Hz, 2H, H21); 1.80–1.22 (m, 24H). **^{13}C APT NMR** (75 MHz, $CDCl_3$, assignments confirmed by HMQC spectrum) δ 96.69 (C2); 86.81 (C9); 75.79 (C10); 62.05 (C6); 54.71 (C8); 34.06 (C22); 32.90 (C21); 30.37; 29.55; 29.47; 29.16; 28.92; 28.82; 28.66; 28.23; 25.46; 19.21; 18.88 (H11). **HMQC** (500 MHz, decoupled, $CDCl_3$, selected data only) δ 4.82 (H2) ↔ δ 96.69 (C2); δ 4.24 (H8) ↔ δ 54.71 (C8); δ 3.85 (H6)↔ δ 62.05 (C6); δ 3.5↔ δ 62.05 (C6); δ 3.41 (H22) ↔ δ 34.06 (C22); δ 2.21 (H11) ↔ δ 18.88 (H11); δ 1.85 (H21) ↔ δ 32.90 (C21). **Anal.** Calcd. for $C_{20}H_{35}O_2Br$: %C, 62.01, %H, 9.11; Found: %C 62.08, %H 9.29.

1,15–Dibromo–2–pentadecyne 166.

163 **166**

To an efficiently stirred solution of triphenylphosphine (0.379 g, 1.446 mmol) in dichloromethane at 0 °C, was added bromine (0.231 g, 1.446 mmol) dropwise. Addition occurs until the first drop not absorbed by the triphenylphosphine, as judged by colour: bromine is rapidly consumed upon addition to form a partially soluble cream–coloured complex with triphenyl phosphine. Once all of the triphenyl phosphine is consumed, the solution takes on the characteristic orange–brown of the bromine. To this stirred suspension at 0 °C is added 2–(15–bromo–pentadec–2–ynyloxy)tetrahydropyran (0.280 g, 0.722 mmol) and the solution allowed to stir and warm to room temperature over a 16 hour period during which time the solution becomes homogeneous. Solvents are removed *in vacuo*, and the residue separated by silica gel column chromatography (eluent: pentane). The target material, 1,15–dibromo–2–pentadecyne, is isolated as a white waxy solid (0.260 g, 99%). Spectroscopic data for **166**: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 4.82 (t, $^5J_{HH}$ = 2.3 Hz, 2H, H1); 3.40 (t, $^3J_{HH}$ = 6.8 Hz, 2H, H15); 2.23 (tt, $^3J_{HH}$ = 7.0 Hz, $^5J_{HH}$ = 2.3 Hz, 2H, H4); 1.85 (tt, $^3J_{HH}$ = 7.0 Hz, $^3J_{HH}$ = 6.8 Hz, 2H, H14); 1.50 (m, 2H); 1.45–1.35 (m, 4H); 1.27 (s, 12H). **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$) δ 88.41;

75.31; 34.09; 32.89; 29.57; 29.55; 29.50; 29.47; 29.12; 28.86; 28.81; 28.41; 28.23; 19.00; 15.84. **Anal.** Calcd. for $C_{15}H_{26}Br_2$: C, 49.20; H, 7.16. Found: C, 49.00; H, 7.25.

1,11–Dibromo–2–undecyne 164.

164

Following the general procedure for the synthesis of **163** above, 1,8–dibromodecane (1.1 g, 4.3 mmol) was added to the liquid ammonia solution of the product of 2–(prop–2–ynyloxy)–tetrahydropyran (0.6 g, 4.5 mmol) and n–BuLi (1.8 mL, 4.5 mmol, 2.5 M). The solution was maintained at –50 °C for 16 hours, then the ammonia was allowed to boil off. The residue was separated by silica gel column chromatography (eluent: hexane). The crude 2–(11–bromo–undeca–2–ynyloxy)–tetrahydropyran was not analytically pure, but the crude material was taken directly to the next step. Thus, the crude 2–(11–bromo–undeca–2–ynyloxy)–tetrahydropyran was dissolved in a minimum of a 1:1 solution of ethanol/THF in a round bottom flask equipped with a reflux condenser, and a catalytic amount of PPTs (25 mg, 0.1 mmol) added to the flask. The solution was maintained at 70 °C for 16 hours. The solvents were removed *in vacuo* and the residue separated by silica gel column chromatography (eluent: 1:1 hexane/ethyl acetate). The product, 11–bromoundeca–2–ynol, was also not characterized, but was

taken directly to the next step. The 11–bromoundeca–2–ynol (0.38 g, 1.54 mmol) was dissolved in ether and the solution cooled to 0 ºC by an ice water bath. To this efficiently–stirred solution was added methanesulfonyl chloride (0.25 g, 2.15 mmol) followed immediately by triethylamine (0.21 g, 2.15 mmol). The solution was allowed to warm slowly to room temperature over a 12 hour period. The solvent volume was reduced *in vacuo*, and the insoluble material removed by filtration through a plug of silica. The filtrate was evaporated to dryness, its mass obtained (0.49 g), then redissolved in dry THF. An excess of lithium bromide (1.32 g, 15.2 mmol) was added as a solid to the flask, and the solution stirred at room temperature for 16 hours. The solution was filtered through a plug of silica gel, then the solvents were evaporated *in vacuo*. The target material, 1,11–dibromo–2–propadecyne, was isolated as a spectroscopically clean yellow oil (0.32 g, 69%). Spectroscopic data for **164**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.93 (t, J = 2.4 Hz, 2H); δ 3.40 (t, J = 6.8 Hz, 2H); δ 2.23 (tt, J = 7.0 Hz, J = 2.4 Hz, 2H); δ 1.85 (quintet, J = 7.1 Hz, 2H); δ1.53–1.28 (m, 10H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 88.2; δ 76.0; δ 33.6; δ 32.9; δ 29.0; δ 28.8; δ 28.7; δ 28.5; δ 28.2; δ 19.0; δ 15.6. **Anal.** Calcd. for $C_{11}H_{18}Br_2$: C, 42.61; H, 5.85. Found: C, 43.31; H, 5.76.

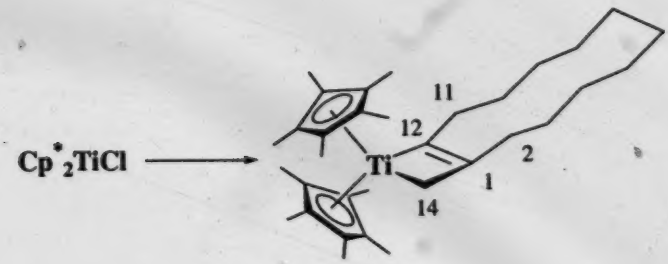
1,13–Dibromo–2–propadecyne 165.

165

Following the general procedure for the synthesis of **163** above, 1,10–dibromodecane (3.0 g, 10 mmol) was added to the liquid ammonia solution of the product of 2–(prop–2–ynyloxy)–tetrahydropyran (1.40g, 10 mmol) and n–BuLi (4.0 mL, 10 mmol, 2.5 M). The solution was maintained at –50 °C for 20 hours, then the ammonia was allowed to boil off. The residue was separated by silica gel column chromatography (eluent: hexane). Starting material 2–(prop–2–ynyloxy)–tetrahydropyran was recovered (1.65g, 55%). The crude 2–(13–bromo–propadec–2–ynyloxy)–tetrahydropyran was not analytically pure, and the crude material was taken directly to the next step. Thus, to an efficiently stirred solution of triphenylphosphine (1.43 g, 5.45 mmol) in dichloromethane at 0 °C, was added bromine (0.87 g, 5.45 mmol) dropwise. Addition occurs until the first drop not absorbed by the triphenylphosphine, as judged by colour: bromine is rapidly consumed upon addition to form a partially soluble cream–coloured complex with triphenyl phosphine. Once all of the triphenyl phosphine is consumed, the solution takes on the characteristic orange–brown of the bromine. To this stirred suspension at 0 °C is added the crude 2–(13–bromo–propadec–2–ynyloxy)–tetrahydropyran and the solution allowed to stir and warm to room temperature over a 16 hour period during which time the

solution becomes homogeneous. Solvents are removed *in vacuo*, and the residue separated by silica gel column chromatography (eluent: hexane). The target material, 1,13–dibromo–2–propadecyne, is isolated as a yellow oil (0.75 g, 81%). Spectroscopic data for **165**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.92 (t, J = 2.4 Hz, 2H); δ 3.40 (t, J = 6.8 Hz, 2H); δ 2.23 (m, 2H); δ 1.86 (quintet, J = 6.8 Hz, 2H); δ1.53–1.32 (m, 12H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 88.2; δ 76.0; δ 33.7; δ 33.0; δ 29.7; δ 29.6; δ 29.3; δ 29.0; δ 28.9; δ 28.6; δ 28.3; δ 19.1; δ 15.6. **Anal.** Calcd for $C_{13}H_{22}Br_2$: C, 46.18; H, 6.56. Found: C, 45.86; H, 6.48.

13,13–Bis(pentamethylcyclopentadienyl)titanabicyclo[10.2.0]–butadeca–1–(12)–ene 167.

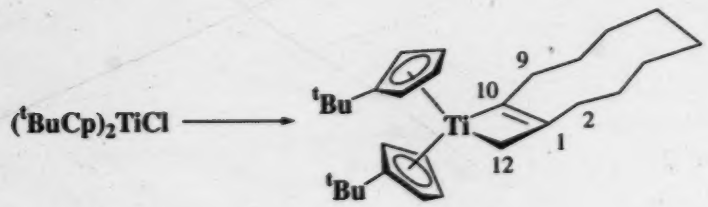


167

To a cold (–35 °C) solution of Cp^*_2TiCl (418 mg, 1.18 mmol) and SmI_2 (0.1 M in THF, 35.5 mL, 3.54 mmol) in dry THF (5 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–35 °C) solution of 1,13–dibromo–2–propadecyne (0.1478 M in THF, 1.18 mmol). The solution was allowed to warm to room

temperature with stirring. After 16h stirring at room temperature, the solution was heated to 80 °C for 6h during which time the colour of the solution turned brown–red. The solvent was removed *in vacuo*. The residue was triturated with pentane and was filtered through a short column of Celite followed by concentration to give an impure brown–red oil (415 mg, 71%). Spectroscopic data for **167**: **^{1}H NMR** (300 MHz, C_6D_6) δ 2.55 (m, 2H, H11); 2.34 (s, 2H, H14); 2.25 (m, 2H, H2); 1.75 (s, 30H, $C_5\underline{Me_5}$); 1.6–1.25 (m, 16H, H3–10). **^{13}C APT NMR** (75 MHz, C_6D_6, assignments confirmed by HMQC, HMBC spectra) δ 212.43 (C12); 117.79 ($\underline{C_5}Me_5$); 105.53 (C1); 78.43 (C14); 35.16 (C11); 32.80 (C2); 31.6–29.5 (C3–10); 12.12 ($C_5\underline{Me_5}$). **HMQC** (300 MHz, decoupled, C_6D_6) δ 2.55 (H11) ↔ δ 35.16 (C11); δ 2.34 (H14) ↔ δ 78.43 (C14); δ 2.25 (H2) ↔ δ 32.80 (C2); δ 1.75 ($C_5\underline{Me_5}$) ↔ δ 12.12 ($C_5\underline{Me_5}$); δ 1.6–1.25 (H3–10) ↔ δ 31.6–29.5 (C3–10). **HMBC** (300 MHz, C_6D_6) δ 2.34 (H14) ↔ δ 105.53 (C1), 12.12 ($C_5\underline{Me_5}$). **HRMS** for $C_{33}H_{52}Ti$ requires *m/z* 496.35486, found *m/z* 496.35633.

11,11–Bis(*tert*–butylcyclopentadienyl)titanabicyclo[8.2.0]–dodeca–1–(10)–ene 168.



168

To a solution of bis(*tert*–butylcyclopentadienyl)titanium (III) chloride (10 mg, 0.031 mmol) and SmI_2 (0.1 M, 0.92 mL, 0.092 mmol) in dry THF at –35 °C was added 1,11–dibromoundec–2–yne (9.5 mg, 0.031 mmol) as a 0.116 M solution in dry THF at –35 °C. The solution was allowed to warm to room temperature and stirred over a 16 hour period at room temperature during which time the solution colour changed from turquoise to brown–red. Solvents were removed *in vacuo* to reveal a brown–red oil (13.5 mg, 99% crude yield of impure material). Spectroscopic data for compound **168**: **^{1}H NMR** (360 MHz, C_6D_6) δ 6.03 (broad singlet); δ 5.49 (broad multiplet, 8H); δ 3.29 (broad multiplet, 2H); δ 2.75 (broad multiplet, 2H); δ 2.10 (broad multiplet, 4H); δ 1.7–1.2 (multiplet, 10H); δ 1.19 (s, 18H, [(C$\underline{H}_3$)$_3$CCpH]); δ 0.90 (broad). **^{13}C (APT) NMR** (100 MHz, C_6D_6) δ 216.7 (C10); 138.77 ([$(CH_3)_3$CCp] *ipso*); 110.58 ([$(CH_3)_3C\underline{C}$p]); 109.94 ([$(CH_3)_3C\underline{C}$p]); 108.98 ([$(CH_3)_3C\underline{C}$p]); 106.25 ([$(CH_3)_3C\underline{C}$p]); 95.26 (C1); 75.23 (C12); 37.65 ([$(CH_3)_3\underline{C}$Cp]); 31.69 ([$(\underline{C}H_3)_3$CCp]); 30.89; 30.24; 29.92; 29.77; 29.42; 28.21. **HRMS** for $C_{29}H_{44}Ti$ requires *m/z* 440.29224, found *m/z* 440.29109.

iv) Intramolecular propargyl radical cyclizations to form bicyclic allenes

1,10–Dibromo–2,8–decadiyne[176,171,172] 171.

171

Ammonia was condensed into a nitrogen–purged three neck round–bottomed flask at –78 °C. Two equivalents of 2–(prop–2–ynyloxy)–tetrahydropyran (18.4 g, 0.13 mol) were added followed by the dropwise addition of two equivalents of n–BuLi (82.2 mL, 0.13 mol, 1.6M). The solution was allowed to stir for one hour over which time it was allowed to warm to –50 °C. 1,4–Dibromobutane (14.2 g, 0.07 mol) was added *via* syringe, and the mixture was stirred and allowed to warm slowly to room temperature over 16 hours under an atmosphere of dry nitrogen over which period the ammonia boiled off, leaving a yellow tar. The residue was separated by silica gel column chromatography (eluent: 20:1 hexane/ethyl acetate). The product, 2–(10–tetrahydropyranyldeca–2,8–diynyloxy)tetrahydropyran (10 g, 0.03 mol) was dissolved in a 1:1 mixture of THF/methanol in a round bottom flask equipped with a reflux condenser. A catalytic amount of PPTs (0.75 g, 0.003 mol 10 mol%) was added to the solution and maintained at 55 °C. After 16 hours, the solution was cooled to room temperature, and the solvents removed *in vacuo*. After silica gel column chromatography (eluent: 10:1 hexane/ethyl acetate), the desired compound 2,8–decadiyndi–(1,10)–ol[205] was recovered as a white solid in 95% yield. Spectroscopic data for 2,8–decadiyndi–(1,10)–ol[176] (consistent with published values): **^{1}H NMR** (360 MHz, $CDCl_3$) δ 4.24 (t, J = 2.1 Hz, 4H); δ 2.24 (m, 4H); 1.60 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 85.8; δ 78.7; δ 51.2; δ 27.5; δ 18.2.

To ether at –5 °C was added sequentially 2,8–decadiyndi–(1,10)–ol (1.00 g, 0.006 mol), toluenesulfonyl chloride (1.20 g, 0.007 mol), and potassium hydroxide (6.70 g, 0.120 mol), and the resulting suspension stirred and allowed to warm to room

temperature over 1 hour. The crude material was filtered through a plug of silica, then the solvent removed *in vacuo*. Spectroscopic data for 1,10–bis(hydroxy–*p*–toluenesulfonate)–2,8–decadiyne: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 7.78 (d, J = 8.3 Hz, 2H); δ 7.73 (d, J = 8.3 Hz, 2H); δ 4.67 (t, J = 2.2 Hz, 2H); δ 2.43 (s, 3H); δ 2.06 (m, 2H); δ 1.40 (m, 2H).

The title compound was synthesized by the exchange of the toluene sulfonate esters for bromide from 1,10–di(hydroxy–*p*–toluenesulfonate)–2,8–decadiyne. Bis–ester 1,10–di(hydroxy–*p*–toluenesulfonate)–2,8–decadiyne (4.0 g, 0.008 mol) was dissolved in THF, and the solution cooled to –30 °C. Excess lithium bromide (29.2 g, 0.336 mol) was added, and the stirred solution allowed to warm to room temperature and stirred for 16 hours, after which spot to spot conversion was noted by silica gel thin layer chromatography. The target material obtained in 90% yield after filtration through celite and removal of the solvent by rotary evaporation. Spectroscopic data for 1,10–dibromo–2,8–decadiyne: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.89 (t, $^5J_{HH}$ = 2.3 Hz, 4H, H1,10); δ 2.25 (m, 4H, H4,7); δ 1.59 (m, 4H, H5,6). **^{13}C {^{1}H} NMR** (75 MHz, $CDCl_3$) δ 87.57; δ 75.77; δ 27.39; δ 18.54; δ 15.61. **ESMS** calculated for $C_{10}H_{12}Br_2 + Ag^+$: 396.8 (35%); 397.8 (5%); 398.8 (100%); 399.8 (12%); 400.8 (97%); 401.8 (12%); 402.8 (35%); 403.8 (5%). Observed: 396.8 (39%); 397.8 (6%); 398.8 (100%); 399.8 (13%); 400.8 (97%); 401.8 (13%); 402.8 (39%); 403.8 (6%).

2,9–Undecadiyn–(1,11)–diol 263.[170,205]

263

Ammonia was condensed at –78 °C into a nitrogen–purged three neck round–bottomed flask fitted with an ammonia condenser connected to a Schlenk line. Sequentially, 2–(prop–2–ynyloxy)–tetrahydropyran (22.4 g, 0.16 mol), and n–BuLi (100 mL, 0.16 mol, 1.6M) were added. The solution was allowed to stir for one hour over which time it was allowed to warm to –50 °C. 1,5–Dibromopentane (16 g, 0.07 mol) was added via syringe, and the mixture was stirred and allowed to warm slowly to room temperature over 16 hours under an atmosphere of dry nitrogen over which time the ammonia was allowed to boil off. The residue was separated by silica gel column chromatography (eluent: 10:1 hexane/ethyl acetate) to afford 2–(11–tetrahydropyranylundeca–2,9–diynyloxy)tetrahydropyran as a spectroscopically clean sample. **Anal.** Calcd. for $C_{21}H_{32}O_4$: %C, 72.38; %H, 9.26. Found: %C, 71.55; %H, 9.27.

To a round bottom flask containing 4 mL of a 1:1 mixture of THF/methanol and equipped with a reflux condenser was added 2–(11–tetrahydropyranylundeca–2,9–diynyloxy)tetrahydropyran (10 g, 0.03 mol). A catalytic amount of PPTs (0.75 g, 0.003 mol 10 mol%) was added to the solution and the solution maintained at 55 °C. After 16

hours, the solution was cooled to room temperature, and the solvents removed *in vacuo*. After silica gel column chromatography (eluent: 10:1 hexane/ethyl acetate), the desired compound 2,9–undecadiyndi–(1,11)–ol[170] was recovered as a spectroscopically clean white solid in 82% yield. Spectroscopic data for 2,9–undecadiyndi–(1,11)–ol **256**: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 4.23 (t, $^5J_{HH}$ = 2.1 Hz, 4H, H1,11); 2.22 (m, 4H, H4,8); 1.51 (m, 6H, H5,6,7). **^{13}C {^{1}H} NMR** (75 MHz, $CDCl_3$) δ 86.19 (C2,10); 78.71 (C3,9); 51.33 (C1,11); 27.90 (C4,8); 27.75 (C6); 18.60 (5,7). **HRMS** $C_{10}H_{13}O_2$ requires *m/z* 165.09155, found *m/z* 165.09039.

1,11–Dibromo–2,9–undecadiyne[170,171,172] 172.

172

To a flask containing 150 mL of Et_2O at –5°C was added 2,9–undecadiyndi–(1,11)–ol (4.03 g, 0.22 mol), followed by powdered potassium hydroxide (24.70 g, 0.440 mol) and toluene sulfonyl chloride (10.07 g, 0.53 mol). The solution was stirred and allowed to warm slowly over 1.5 hours, after which time spot to spot conversion was noted by silica gel thin layer chromatography. The reaction solution was filtered through silica gel and the solvents evaporated by rotary evaporation. Crude yield: 89%. The crude material was carried through to the next step. Spectroscopic data for 1,11–bis(hydroxy–*p*–

toluenesulfonate)–2,9–undecadiyne: **^{1}H NMR** (30 MHz, $CDCl_3$) δ 7.80 (ddd, J = 8.4 Hz, J =1.9 Hz, J = 1.8 Hz, 2H); δ 7.32 (ddd, J = 8.4 Hz, J = 0.6 Hz, J = 0.5 Hz, 2H); δ 4.68 (t, J = 2.2 Hz, 2H); δ 2.43 (s, 3H); δ 2.06 (tt, J = 6.7 Hz, J = 2.2 Hz, 2H); δ 1.32 (m, 3H).

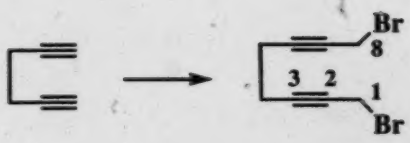
The crude 1,11–bis(hydroxy–*p*–toluenesulfonate)–2,9–undecadiyne (9.58 g, 0.02 mol) was dissolved in dry THF at –30 °C. To the solution was added lithium bromide (35 g, 0.40 mol). The solution was stirred and allowed to warm to room temperature over a 16 hour period. The resulting solution was filtered through silica, and the solvents removed *in vacuo* to afford 1,11–dibromo–2,9–undecadiyne **172** as an analytically pure yellow oil in 100% yield. Spectroscopic data for 1,11–dibromo–2,9–undecadiyne: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.89 (t, $^5J_{HH}$ = 2.5 Hz, 4H, H1,11); δ 2.21 (m, 4H, H4,8); δ 1.47 (m, 6H, H5,6,7). **^{13}C {^{1}H} NMR** (75 MHz, $CDCl_3$) δ 87.75; δ 75.47; δ 27.77; δ 27.68; δ 18.72; δ 15.63. **Anal.** Calcd. for $C_{11}H_{14}Br_2$: C, 43.17; H, 4.61. Found: C, 43.18; H, 4.80.

1,9–Dibromo–2,7–nonadiyne[171,172] 170.

170

Ammonia was condensed into a nitrogen–purged three neck round–bottomed flask at –78 °C. Two equivalents of 2–(prop–2–ynyloxy)–tetrahydropyran (16.4 g, 0.11 mol) were added followed by the dropwise addition of two equivalents of n–BuLi (72.0 mL, 0.11 mol, 1.6M) followed by the removal of the –78 °C bath. The solution was allowed to stir for one half hour, after which 1,3–dibromobutane (9.4 g, 0.05 mol) was added *via* syringe, and the mixture was stirred and allowed to warm slowly to room temperature over 16 hours under an atmosphere of dry nitrogen over which period the ammonia boiled off. The crude material was purified by bulb–to–bulb distillation (65 °C, < 1mmHg), to afford impure 2–(9–tetrahydropyranyldnona–2,7–diynyloxy)tetrahydropyran (crude yield: 77%). To a stirred dichloromethane solution of triphenylphosphine (2.58 g, 7.94 mmol) at 0 °C was added dropwise bromine (1.26 g, 7.94 mmol) until the first drop persisted. To the resultant creamy yellow suspension was added crude 2–(9–tetrahydropyranyldnona–2,7–diynyloxy)tetrahydropyran (578 mg, 1.80 mmol) and the reaction mixture allowed to warm to room temperature over 16 hours. The solvents were removed *in vacuo* and the crude material purified by silica gel chromatography (eluent: pentane) to afford the title compound as a yellow oil in 33% yield. Spectroscopic data for 1,9–dibromo–2,7–nonadiyne[176] (consistent with published values) **170.**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.40 (t, J = 2.2 Hz, 4H); δ 1.94 (tt, J = 7.0 Hz, J = 2.2 Hz, 4H); δ 1.29 (quintet, J = 7.0 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 86.8; δ 76.6; δ 27.3; δ 18.1; δ 15.3.

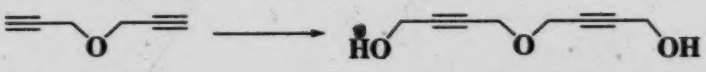
1,8–Dibromo–2,6–octadiyne[173] 175.



175

1,5–Hexadiyne (1.6 g, 20.5 mmol) was dissolved in 40 mL of dry THF and the solution cooled to –40 °C under a nitrogen blanket. By cannula, n–BuLi (28 mL, 45.0 mmol, 1.6M) was added to the flask and the cold bath removed and the solution stirred for 30 minutes. Paraformaldehyde (1.47 g, 49 mmol) was added as a THF solution. The solution was heated to 70 °C and maintained at that temperature for 16 hours. The volume of the reaction mixture was reduced and filtered through silica gel. The crude filtrate was recrystallized from boiling benzene to afford a white solid (0.69 g, 24%). This material was dissolved in dry ether (30 mL) and the solution cooled to 0 °C. To this stirred solution was added phosphorous tribromide (1.35 g, 5.00 mmol) and the solution allowed to warm to room temperature over 16 hours. The solvents were removed *in vacuo*, and the residue purified by silica gel chromatography (eluent: hexane) to afford 1,8–dibromo–2,6–octadiyne[173] as a spectroscopically pure oil in 27 % yield. Spectroscopic data for **175**: **^{1}H NMR** (500 MHz, $CDCl_3$) δ 3.38 (t, J = 0.5 Hz, 4H); δ 1.93 (t, J = 0.5 Hz, 4H). **^{13}C NMR** (125 MHz, $CDCl_3$) δ 85.9; δ 77.0; δ 18.8; δ 15.1. **Anal.** Calcd. for $C_8H_8Br_2$: C, 36.40; H, 3.05. Found: C, 37.21, H, 3.00.

4–(4–Hydroxy–but–2–ynyloxyl)–but–2–yn–1–ol[176] 177.



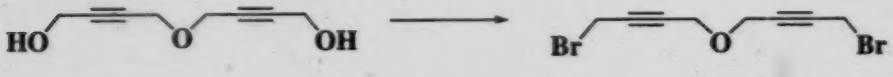
177

Volatile 3–(prop–2–ynyloxyl)–prop–1–yne was synthesized in the following manner: Sodium hydroxide (30 g, 0.75 mol) was ground in a pestle and added to a mixture of propargyl bromide (59.5 g, 0.5 mol) and propargyl alcohol (39.2 g, 0.7 mol). The sodium hydroxide must be added slowly: the reaction is very exothermic. The solution was stirred for one hour, then quenched with water, and extracted into ether. The volatile propargyl ether[174] was distilled (50 °C @ 50 mm/Hg), and recovered in 32% yield.

Freshly distilled 3–(prop–2–ynyloxyl)–prop–1–yne (15 g, 0.16 mol) was dissolved in dry THF in a nitrogen–purged Schlenk flask fitted with a rubber septum, and cooled to –78 °C. A slight excess of n–BuLi (220 mL, 0.35 mol, 1.6M) was slowly added *via* cannula and the solution stirred at –78 °C for one hour. A white precipitate was formed. Excess *para*–formaldehyde (48 g, 1.60 mol) was added as a powder under a nitrogen blanket, and the reaction solution was allowed to warm to room temperature. The rubber septum was replaced, and the solution was maintained at 50 °C for 16 hours. The reaction was worked up by rotary evaporation of the solvent, followed by distillation under reduced pressure to afford the crude product 4–(4–hydroxy–but–2–ynyloxyl)–but–2–yn–1–ol[176]. The crude product was recrystallized from boiling chloroform to afford an off–white spectroscopically clean powder (9.4 g, 45%). Spectroscopic data for 4–(4–hydroxy–but–2–ynyloxyl)–but–2–yn–1–ol **177**: **^{1}H NMR** (300 MHz, $(CD_3)_2CO$) δ 4.32

(broad singlet, 2H); δ 4.21 (broad singlet, 8H). **^{13}C {^{1}H} NMR** (75 MHz, $(CD_3)_2CO$) δ 86.89; δ 80.34; δ 56.91; δ 50.43. **Anal.** Calcd. for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 61.56; H 6.57.

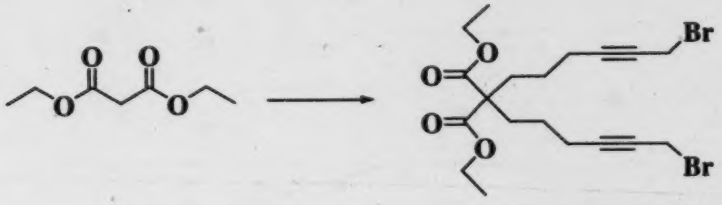
1–Bromo–4–(4–bromo–but–2–ynyloxy)–but–2–yne[176] 178.



178

4–(4–Hydroxy–but–2–ynyloxyl)–but–2–yn–1–ol (4.80 g, 31.1 mmol) was stirred in dry diethyl ether in a Schlenk flask under a dry nitrogen atmosphere at 0 °C. Phosphorous tribromide (8.42 g, 31.1 mmol) and pyridine (0.24 g, 3.1 mmol) were added and the solution immediately warmed to room temperature. The reaction was stirred for 16 hours at room temperature. Target material 1–bromo–4–(4–bromo–but–2–ynyloxy)–but–2–yne was recovered in 60% yield (5.2 g) after silica gel chromatography (eluent: hexane). Spectroscopic data for 1–bromo–4–(4–bromo–but–2–ynyloxy)–but–2–yne[176] **178**: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 4.28 (t, $^{5}J_{HH}$ = 2.0 Hz, 4H); δ 3.94 (t, $^{5}J_{HH}$ = 2.0 Hz, 4H). **^{13}C APT NMR** (125 MHz, $CDCl_3$) δ 82.06; δ 81.89; δ 57.03; 14.07. **ESMS** isotope pattern for $C_8H_8OBr_2 + Ag^+$ calc. 384.8 (35%); 385.8 (5%); 386.8 (100%); 387.8 (10%); 388.8 (95%); 389.8 (10%); 390.8 (35%), observed 384.8 (35%); 385.8 (5%); 386.8 (100%); 387.8 (10%); 388.8 (95%); 389.8 (10%); 390.8 (35%).

2,2–Bis–(6–bromo–hex–4–ynyl)–malonic acid diethyl ester 190.



190

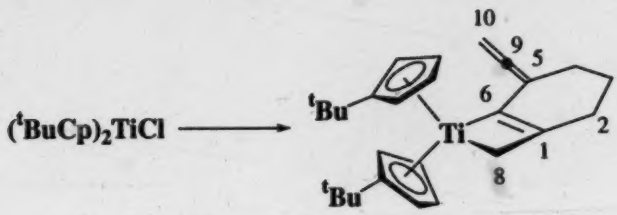
To a room temperature solution of diethyl malonate (272 mg, 1.7 mmol) in 3:1 THF/DMPU was added sodium hydride (47 mg, 1.9 mmol). The mixture was stirred until the solution went clear. 2–(6–Iodo–2–hexynyloxy)tetrahydropyran[28] (500 mg, 1.6 mmol) was added and the solution stirred at room temperature for one hour. Then sodium hydride (46.7 mg, 1.9 mmol) was added and the solution stirred until it went clear (approximately 15 minutes). Finally, 2–(6–iodo–2–hexynyloxy)tetrahydropyran was added and the solution stirred at room temperature for 16 hours. Separation of the crude material by silica gel chromatography (eluent: 10:1 hexane/ethyl acetate) afforded the desired product in 79% yield. Spectroscopic data for 2,2–bis–(6–tetrahydropyranyl–hex–4–ynyl)–malonic acid diethyl ester: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 4.79 (t, J = 3.3 Hz, 2H); δ 4.21 (qt, J = 15.2 Hz, J = 2.1 Hz, 4H); δ 4.21 (m); δ 3.83 (m, 2H); δ 3.53 (m, 2H); δ 2.22 (tt, J = 7.1 Hz, J = 2.1 Hz, 4H); δ 1.95 (m, 4H); δ 1.72 (m, 4H); δ 1.57 (m, 8H); δ 1.41 (m, 4H); δ 1.24 (t, J = 7.1 Hz, 6H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.4; δ 96.7; δ 85.7; δ 62.0; δ 61.2; δ 54.6; δ 31.7; δ 30.3; δ 25.4; δ 23.5; δ 19.1; δ 14.1.

To a 1:1 solution of ethanol and THF in a round bottom flask equipped with a reflux condenser was added 2,2–bis–(6–tetrahydropyranyl–hex–4–ynyl)–malonic acid

diethyl ester (669 mg, 1.3 mmol) at room temperature. A catalytic amount of PPTs (50 mg, 0.2 mmol) was added, and the solution maintained at 70 °C for 48 hours. The solvents were remove *in vacuo* and the residue separated by silica gel column chromatography (eluent: 10:1 hexane/ethyl acetate). The major fraction was collected, and the uncharacterized material dissolved in a minimum of THF. An excess of methane sulfonyl chloride (0.53 g, 4.68 mmol) was added, followed by an excess of triethyl amine (0.52 g, 5.20 mmol). The resultant suspension was stirred for 16 hours at room temperature. The crude material was taken directly to the bromination step. The crude bis–sulfonate ester was dissolved in THF at room temperature, and lithium bromide (1.1 g, 13 mmol) was added. The solution was stirred for 16 hours at room temperature. The target material, 2,2–bis–(6–bromo–hex–4–ynyl)–malonic acid diethyl ester **190**, was obtained in 87% yield (0.54 g, 1.13 mmol) after silica gel chromatography. Spectroscopic data for 2,2–bis–(6–bromo–hex–4–ynyl)–malonic acid diethyl ester: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 4.19 (quartet, $^{3}J_{HH}$ = 7.1 Hz, 4H); δ 3.91 (t, $^{5}J_{HH}$ = 2.4 Hz, 4H); δ 2.25 (tt, $^{3}J_{HH}$ = 6.9, $^{5}J_{HH}$ = 2.4 Hz, 4H); δ 1.96 (2nd order, 4H); δ 1.44 (2nd order, 4H); δ 1.25 (t, $^{3}J_{HH}$ = 7.1 Hz, 6H). **^{13}C {^{1}H} NMR** (75 MHz, $CDCl_3$) δ 171.31; δ 87.16; δ 75.87; δ 61.21; δ 56.95; δ31.45; δ 23.13; δ 19.19; δ 15.43; δ 14.10. **HRMS** $C_{19}H_{26}O_4{}^{81}Br_2$ requires *m/z* 480.01569, found *m/z* 480.01732; $C_{19}H_{26}O_4{}^{79}Br{}^{81}Br$ requires *m/z* 478.01773, found *m/z* 478.01592; $C_{19}H_{26}O_4{}^{81}Br$ requires *m/z* 399.09940, found *m/z* 399.09984; $C_{19}H_{26}O_4{}^{79}Br$ requires *m/z* 397.10144, found *m/z* 397.10178.

7,7–Bis(*tert*–butylcyclopentadienyl)titanabicyclo[4.2.0]–2–allenyl–octa–1–(6)–ene

181.

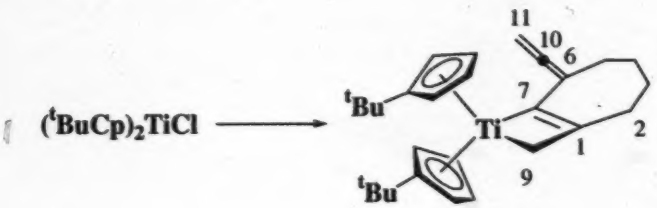


181

To a cold (–35 °C) solution of (^{t}BuCp)$_2$TiCl (340 mg, 1.04 mmol) and SmI_2 (0.1 M in THF, 31.4 mL, 3.14 mmol) in dry THF (5 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–35 °C) solution of 1,9–dibromo–2,7–nonadiyne (0.120 M in THF, 1.04 mmol). The solution was allowed to warm to room temperature with stirring. After 16 hours stirring at room temperature, during which time the colour of the solution turned blood red, the solvent was removed *in vacuo*. The residue was triturated with pentane and was filtered through a short column of celite followed by concentration to give a spectroscopically clean red solid (390 mg, 92 %). Spectroscopic data for **181**: **^{1}H NMR** (360 MHz, C_6D_6) δ 5.82 (s, 2H, ^{t}BuC$_5$H$_4$); 5.69 (s, 2H, ^{t}BuC$_5$H$_4$); 5.45 (s, 2H, ^{t}BuC$_5$H$_4$); 5.33 (s, 2H, ^{t}BuC$_5$H$_4$); 4.97 (s, 2H, H10); 3.21 (s, 2H, H8); 2.57 (s, 2H, H3); 2.43 (s, 2H, H5); 1.60 (s, 2H, H4); 1.09 (s, 18H, ^{t}BuC$_5$H$_4$). **^{13}C (APT) NMR** (125 MHz, C_6D_6, assignments confirmed by HMQC spectrum) δ 220.88 (C6); 210.43 (C9); 140.25 (^{t}BuC$_5$H$_4$ ipso); 110.30 (^{t}BuC$_5$H$_4$ ring); 109.81 (^{t}BuC$_5$H$_4$ ring); 109.67 (^{t}BuC$_5$H$_4$ ring); 108.46 (^{t}BuC$_5$H$_4$ ring); 100.75 (C2); 94.38 (C1); 76.50 (C10); 67.96 (C8); 36.70 (C3); 32.70 (^{t}BuC$_5$H$_4$); 31.61 (^{t}BuC$_5$H$_4$) ; 28.57 (C5);

24.99 (C4). **HMQC** (500 MHz, decoupled, C_6D_6) δ 5.82 ($^tBuC_5\underline{H}_4$) ↔ δ 110.30 ($^tBu\underline{C}_5H_4$ ring); δ 5.69 ($^tBuC_5\underline{H}_4$) ↔ δ 109.67 ($^tBu\underline{C}_5H_4$ ring); δ 5.45 ($^tBuC_5\underline{H}_4$) ↔ δ 109.81 ($^tBu\underline{C}_5H_4$ ring); δ 5.46 ($^tBuC_5\underline{H}_4$) ↔ δ 108.46 ($^tBu\underline{C}_5H_4$ ring); δ 4.97 (H10) ↔ δ 76.50 (C10); δ 3.21 (H8) ↔ δ 67.96 (C8); δ 2.57 (H3) ↔ δ 36.70 (C3); δ 2.43 (H5) ↔ δ 28.57 (C5); δ 1.60 (H4) ↔ δ 24.99 (C4); δ 1.09 ($^t\underline{Bu}C_5H_4$) ↔ δ 31.61 ($^t\underline{Bu}C_5H_4$). **HRMS** for $C_{27}H_{36}Ti$ requires *m/z* 408.22964, found *m/z* 408.22977.

8,8–Bis(*tert*–butylcyclopentadienyl)titanabicyclo[5.2.0]–2–allenyl–non–1–(7)–ene 180.



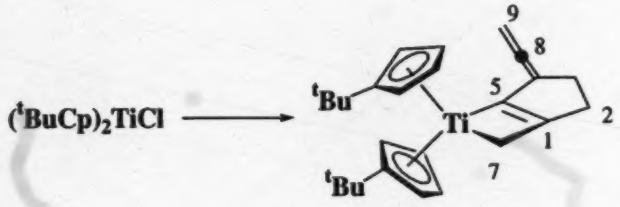
180

To a cold (–35 °C) solution of (^{t}BuCp)$_2$TiCl (20 mg, 0.061 mmol) and SmI_2 (0.1 M in THF, 1.83 mL, 0.183 mmol) in dry THF (5 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–35 °C) solution of 1,10–dibromo–2,8–decadiyne (0.10 M in THF, 0.061 mmol). The solution was allowed to warm to room temperature with stirring. After 16 hours stirring at room temperature, during which time the colour of the solution turned blood red, the solvent was removed *in vacuo*. The residue was triturated with pentane and was filtered through a short column of celite followed by concentration to give a spectroscopically clean red solid (21 mg, 81%).

Spectroscopic data for **180**: **^{1}H NMR** (500 MHz, C_6D_6) δ 5.89 (s, 2H, ^{t}BuC$_5$H$_4$); 5.62 (s, 2H, ^{t}BuC$_5$H$_4$); 5.57 (s, 2H, ^{t}BuC$_5$H$_4$); 5.46 (s, 2H, ^{t}BuC$_5$H$_4$); 4.85 (s, 2H, H11); 3.26 (s, 2H, H9); 2.58 (s, 3H, H3); 2.38 (s, 3H, H6); 1.70 (s, 4H, H4,5); 1.10 (s, 18H, ^{t}BuC$_5$H$_4$). **^{13}C (APT) NMR** (125 MHz, C_6D_6, assignments confirmed by HMQC, and HMBC spectra) δ 219.69 (C7); 211.93 (C10); 138.92 (^{t}BuC$_5$H$_4$ ipso); 111.35 (^{t}BuC$_5$H$_4$ ring); 111.03 (^{t}BuC$_5$H4 ring); 110.15 (^{t}BuC$_5$H$_4$ ring); 107.87(^{t}BuC$_5$H$_4$ ring); 104.12 (C2); 96.24 (C1); 75.23 (C11); 71.62 (C9); 37.09 (C6); 32.93 (C3); 32.54 (^{t}BuC$_5$H$_4$) ; 31.68 (^{t}BuC$_5$H$_4$); 28.93 (C4); 28.40 (C5). **HMQC** (500 MHz, decoupled, C6D6) δ 5.89 (^{t}BuC$_5$H$_4$) ↔ δ 111.35 (^{t}BuC$_5$H$_4$ ring); δ 5.62 (^{t}BuC$_5$H$_4$) ↔ δ 111.03 (^{t}BuC$_5$H$_4$ ring); δ 5.57 (^{t}BuC$_5$H$_4$) ↔ δ 110.15 (^{t}BuC$_5$H$_4$ ring); δ 5.46 (^{t}BuC$_5$H$_4$) ↔ δ 107.87 (tBuC$_5$H$_4$ ring); δ 4.85(H11) ↔ δ 75.23 (C11); δ 3.26 (H9) ↔ δ 71.62 (C9); δ 2.58 (H3) ↔ δ 37.09 (C3); δ 2.38 (H6) ↔ δ 32.93 (C6); δ 1.70 (H4,5) ↔ δ 28.93 (C4), 28.40 (C5); δ 1.10 (^{t}BuC$_5$H$_4$) ↔ δ 31.68 (^{t}BuC$_5$H$_4$). **HMBC** (500 MHz, C_6D_6) δ 5.89 (^{t}BuC$_5$H$_4$) ↔ δ 138.92 (^{t}BuC$_5$H$_4$ ipso), 111.03 (^{t}BuC$_5$H$_4$ ring), 107.87 (^{t}BuC$_5$H$_4$ ring); δ 5.62 (^{t}BuC$_5$H$_4$) ↔ δ 138.92 (^{t}BuC$_5$H$_4$ ipso), 111.03 (^{t}BuC$_5$H$_4$ ring), 107.87 (^{t}BuC$_5$H$_4$ ring); δ 5.57 (^{t}BuC$_5$H$_4$) ↔ δ 138.92 (^{t}BuC$_5$H$_4$ ipso), 111.03 (^{t}BuC$_5$H$_4$ ring), 107.87 (^{t}BuC$_5$H$_4$ ring); δ 5.46 (^{t}BuC$_5$H$_4$) ↔ δ 138.92 (^{t}BuC$_5$H$_4$ ipso), 111.03 (^{t}BuC$_5$H$_4$ ring); δ 4.85 (H11) ↔ δ 219.69 (C7), 211.93 (C10), 104.12 (C2), 96.24 (C1), 32.93 (C3), 28.93 (C4); δ 3.26 (H9) ↔ δ 219.69 (C7), 104.12 (C2), 96.24 (C1); δ 1.10 (^{t}BuC$_5$H$_4$) ↔ δ 138.92 (^{t}BuC$_5$H$_4$ ipso), 32.54 (^{t}BuC$_5$H$_4$), 31.68 (^{t}BuC$_5$H$_4$). **HRMS** for $C_{28}H_{38}Ti$ requires *m/z* 422.24530, found *m/z* 422.24554.

8,8–Bis(*tert*–butylcyclopentadienyl)titanabicyclo[3.2.0]–2–allenyl–non–1–(5)–ene

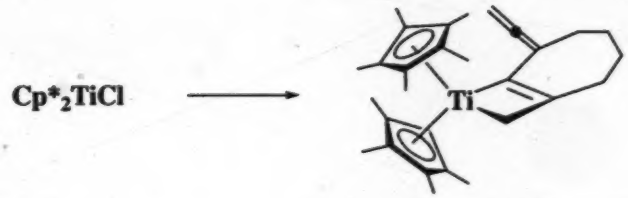
182.



182

To a cold (–35 °C) solution of (^{t}BuCp)$_2$TiCl (30 mg, 0.092 mmol) and SmI_2 (0.1 M in THF, 1.83 mL, 0.183 mmol) in dry THF (5 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–35 °C) solution of 1,8–dibromo–2,6–octadiyne (0.144 M in THF, 0.046 mmol), and the solution maintained at –35 °C for one minute. To this solution was added 2–iodopropane (15.6 mg, 0.092 mmol), and the solution maintained at –35 °C for one minute. Next, SmI_2 (0.1 M in THF, 0.92 mL, 0.09 mmol) was added and the solution maintained at –35 °C for 16 hours. After 16 hours, during which time the colour of the solution turned blood red, the solvent was removed *in vacuo*. The residue was triturated with pentane and was filtered through a short column of celite followed by concentration to give a red oil (unquantified). Spectroscopic data for **182**: **^{1}H NMR** (360 MHz, C_6D_6) δ 5.78 (s, 2H); δ 5.55 (s, 2H); δ 5.42 (s, 2H); δ 5.35 (s, 2H); δ 5.20 (s, 1H); δ 4.92 (s, 1H); δ 3.40; δ 3.05 (s, 2H); δ 1.06 (s, 18H). **^{13}C NMR** (75 MHz, C_6D_6) δ 224.2; δ 140.1; δ 137.4; δ 130.0; δ 129.0; δ 110.7; δ 110.2; δ 109.4; δ 108.2; δ 97.7; δ 62.8; δ 39.6; δ 32.8; δ 31.4

8,8–Bis(pentamethylcyclopentadienyl)titanabicyclo[5.2.0]–2–allenyl–non–1–(7)–ene 187.

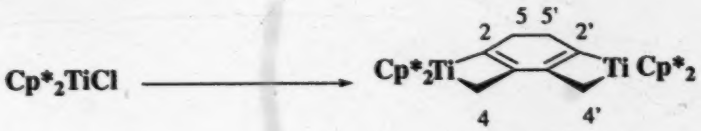


187

To a cold (–35 °C) solution of Cp^*_2TiCl (11.8 mg, 0.033 mmol) and SmI_2 (0.1 M in THF, 1.0 mL, 0.10 mmol) in dry THF (1 mL) in a thick–walled glass reaction vessel with removable Teflon© stopcock was added a cold (–67 °C) solution of 1,10–dibromo–2,8–decadiyne (0.114 M in THF, 0.033 mmol). The solution was allowed to warm to room temperature with stirring over 16 hours, during which time the colour of the solution turned blood red. The solvent was removed *in vacuo*, and the residue was triturated with pentane and was filtered through a short column of celite followed by concentration to give an impure red oily solid (13.2 mg, 89%). Spectroscopic data for **187**: **^{1}H NMR** (360 MHz, C_6D_6) δ 4.88 (s, 2H); δ 2.50 (broad singlet, 3H); δ 2.37 (m, 6H); δ 1.71 (s, 30H). **^{13}C NMR** (75 MHz, C_6D_6) δ 216.1; δ 211.9; δ 118.4; δ 104.8; δ 101.7; δ 76.6; δ 74.4; δ 34.3; δ 34.0; δ 30.1; δ 29.1; δ 11.9.

v) Intramolecular ligand-ligand coupling reactions

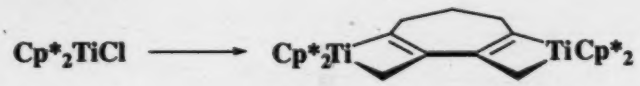
[1,2:3,4–Bis(2,2'–bis(pentamethylcyclopentadienyl)titanacyclobuteno]-cyclohexadiene 197.



197

A solution of two equivalents of 1,1–bis(pentamethylcyclopentadienyl)titanium chloride (76.4 mg, 0.21 mmol), and four equivalents of SmI_2 (0.1M, 4.3 mL, 0.43 mmol) in THF was cooled to –35 °C. One equivalent of 1,8–dibromo–2,6–octadiyne (0.10 mmol) was added and the solution allowed to warm to room temperature with stirring over a 12 hour period. The solvent was removed *in vacuo*, and the residue was triturated with pentane and was filtered through a short column of celite followed by concentration to yield **197** as a brown solid (110 mg, 76%). Compound **197** is unstable even at –35 °C, and all attempts to grow crystals suitable for X–ray analysis failed. Spectroscopic data for **197**: **^{1}H NMR** (400 MHz, C_6D_6) δ 2.59 (broad singlet, 4H, H5,5'); 2.50 (broad singlet, 4H, H5,5'); 1.82 (s, 60H, $(CH_3)_5C_5$). **^{13}C NMR** (100 MHz, C_6D_6, assignments confirmed by HMQC spectrum) δ 219.55 (s, C2, 2'); 117.37 (s, $(CH_3)_5C_5$); 96.14 (s, C3,3'); 76.40 (t, $^1J_{CH}$ = 135.5 Hz, C4,4'); 35.14 (t, $^1J_{CH}$ = 126.0 Hz, C5,5'); 12.29 (q, $^1J_{CH}$ = 125.0 Hz, $(CH_3)_5C_5$). **HMQC** (300 MHz, C_6D_6) δ 2.59 (H5,5') ↔ δ 35.14 (C5,5'); δ 2.50 (H4,4') ↔ 76.40 (C4,4'); δ 1.82 ($(CH_3)_5C_5$) ↔ 12.29 ($(CH_3)_5C_5$).

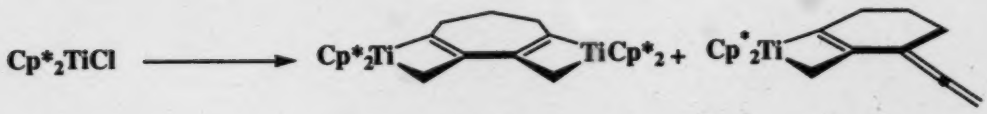
[1,2:3,4–Bis(2,2'–bis(pentamethylcyclopentadienyl)titanacyclobuteno]-cycloheptadiene 198.



198

A solution of four equivalents of 1,1–bis(pentamethylcyclopentadienyl)titanium(III) chloride (200 mg, 0.565 mmol), and six equivalents of SmI_2 (0.1M, 4.3 mL, 0.43 mmol) in THF was cooled to –67 °C. One equivalent of 1,9–dibromo–2,7–nonadiyne (1.40 mL, 0.141 mmol, 0.1M) was added and the solution allowed to warm to room temperature with stirring over a 16 hour period. The solvent was removed *in vacuo*, and the residue was triturated with pentane and was filtered through a short column of celite followed by concentration to yield **198** as an impure brown oil (82 mg, 77%). Spectroscopic data for **198**: **^{1}H NMR** (360 MHz, C_6D_6) δ 2.54 (broad multiplet, 2H); δ 2.40 (s, 2H); δ 1.84 (s, 1H); δ 1.82 (s, 60H). **^{13}C NMR** (100 MHz, C_6D_6) δ 218.4 (s); δ 117.7 (s); δ 97.2 (s); δ 80.5 (t, $^2J_{HC}$ = 135 Hz); δ 37.6 (t, $^2J_{HC}$ = 89 Hz); δ 12.5 (quintet, $^2J_{HC}$ = 139 Hz); δ 12.3 (quartet, $^2J_{HC}$ = 126 Hz).

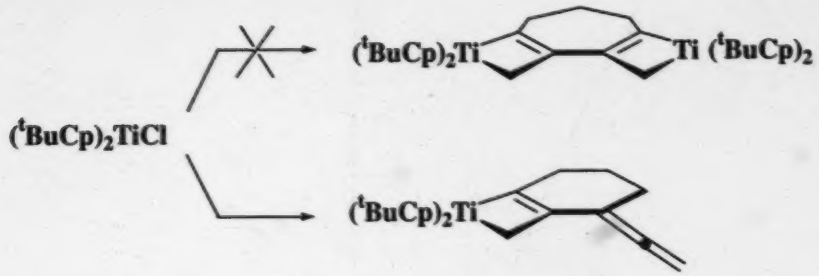
Mixture of [1,2:3,4–Bis(2,2'–bis(pentamethylcyclopentadienyl)-titanacyclobuteno]cycloheptadiene 198 and 7,7–bis(pentacyclopentadienyl)-titanabicyclo[4.2.0]–2–allenyl–octa–1–(6)–ene 187.



198 **187**

A solution of two equivalents of 1,1–bis(pentamethylcyclopentadienyl)titanium(III) chloride (10 mg, 0.028 mmol), and four equivalents of SmI_2 (0.1M, 0.56 mL, 0.056 mmol) in THF was cooled to –35 °C. One equivalent of 1,9–dibromo–2,7–nonadiyne (0.14 mL, 0.014 mmol, 0.1M) was added and the solution maintained at –35 °C for 30 minutes, then allowed to warm to room temperature with stirring over a 16 hour period. The solvent was removed *in vacuo*, and the residue was triturated with pentane and was filtered through a short column of celite followed by concentration to yield **198** and **187** as an approximate 3:1 ratio. Spectroscopic data for the mixture: **^{1}H NMR** (500 MHz, C_6D_6) δ 5.00 (s); δ 2.83 (broad multiplet); δ 2.54 (t, J = 7.5 Hz); δ 2.41 (s); δ 2.11 (quintet, J = 7.5 Hz); δ 2.06 (s); δ 1.82 (s); δ 1.70 (s). **^{13}C NMR** (125 MHz, C_6D_6) δ 217.1; δ 128.5; δ 117.9; δ 117.6; δ 96.7; δ 80.0; δ 69.4; δ 40.4; δ 37.4; δ 34.0; δ 30.0; δ 28.0; δ 12.2; δ 12.0. **HRMS** for $C_{29}H_{40}Ti$ requires *m/z* 436.26096, found *m/z* 436.26069.

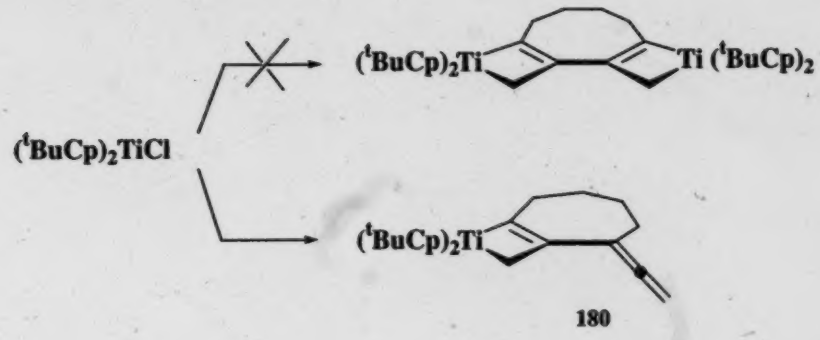
Attempted synthesis of [1,2:3,4–Bis(2,2'–bis(*tert*-butylcyclopentadienyl)-titanacyclobuteno]cycloheptadiene.



181

To a cold (–35 °C) THF solution of two equivalents of bis(*tert*–butylcyclopentadienyl)titanium(III) chloride (20 mg, 0.061 mmol) and four equivalents of samarium diiodide (1.22 mL, 0.122 mmol, 0.1 M) was added a THF solution of 1,9–dibromo–2,7–nonadiyne (0.31 mL, 0.031 mmol, 0.1 M). The solution was stirred and allowed to warm to room temperature over a 16 hour period. The solvent was removed *in vacuo*, and the residue was triturated with pentane and was filtered through a short column of celite followed by concentration to reveal 7,7–bis(*tert*–butylcyclopentadienyl)titanabicyclo[4.2.0]–2–allenyl–octa–1–(6)–ene **181** (*vide supra*) in 94% yield (based on 1,9–dibromo–2,7–nonadiyne).

Attempted synthesis of [1,2:3,4–Bis(2,2'–bis(*tert*–butylcyclopentadienyl)-titanacyclobuteno]cyclooctadiene.

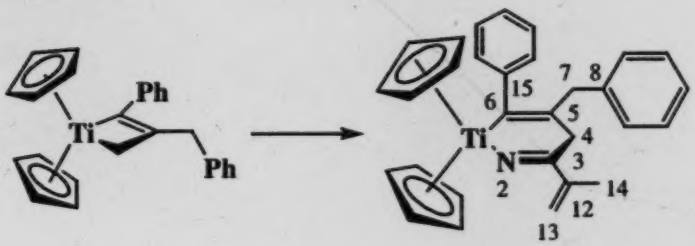


180

To a cold (–35 °C) THF solution of two equivalents of bis(*tert*–butylcyclopentadienyl)titanium(III) chloride (10 mg, 0.031 mmol) and four equivalents of samarium diiodide (0.61 mL, 0.061 mmol, 0.1 M) was added a THF solution of 1,10–dibromo–2,8–decadiyne (0.25 mL, 0.015 mmol, 0.062 M). The solution was stirred and allowed to warm to room temperature over a 16 hour period. The solvent was removed *in vacuo*, and the residue was triturated with pentane and was filtered through a short column of celite followed by concentration to reveal 8,8–bis(*tert*–butylcyclopentadienyl)titanabicyclo[5.2.0]–2–allenyl–non–1–(7)–ene **180** (*vide supra*) in 66% yield (based on 1,10–dibromo–2,8–decadiyne).

vi) Functionalization of titanacyclobutene complexes.

1,1–Bis(cyclopentadienyl)–5–benzyl–3–isopropenyl–6–phenyltitanacyclo–1–azahexa–2,5–diene 230.

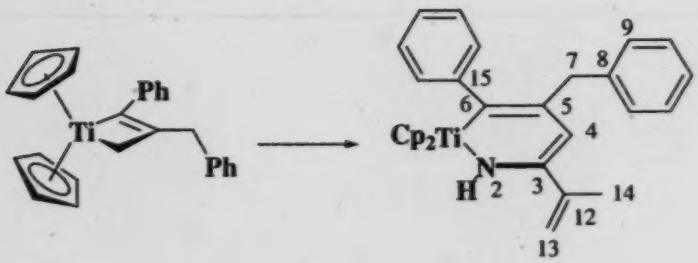


230

To a solution of 1,1–bis(cyclopentadienyl)–3–benzyl–2–phenyltitanacyclobutene **107** (93mg, 0.24 mmol) in toluene at room temperature in a thick–walled glass reaction vessel with removable Teflon© stopcock was added isopropenyl nitrile (17.8 mg, 0.26 mmol). The solution was stirred at room temperature for sixteen hours during which time the red solution turned brown. Evaporation of solvent under reduced pressure followed by recrystallization from hexane at –35 °C gave 1,1–bis(cyclopentadienyl)–5–benzyl–3–isopropenyl–4–phenyltitanacyclo–1–azahexene **230** (91 mg, 84%) as a red powder. Spectroscopic data for **230**: **^{1}H NMR** (360 MHz, C_6D_6) δ 7.19 (m, 6H, Ar<u>H</u>); 7.15–6.9 (m, 4H, Ar<u>H</u>, obscured by C_6D_6); 5.55 (s, 10H, <u>Cp</u>); 4.93 (t, $^2J_{HH}$ = 0.9 Hz, 1H, =C<u>H</u>$_2$); 4.90 (qd, $^4J_{HH}$ = 1.0 Hz, $^2J_{HH}$ = 0.9 Hz, 1H, =C<u>H</u>$_2$); 3.49 (s, 2H, H4); 3.33 (s, 2H, H7); 1.74 (t, $^4J_{HH}$ = 1.0 Hz, 3H, C<u>H</u>$_3$). **^{13}C {^{1}H} NMR** (75 MHz, C_6D_6, assignments confirmed by HMBC spectrum) δ 187.87 (C6); 163.66 (C3); 154.94 (phenyl *ipso*); 143.60 (C8);

140.94 (C12); 128.67 (Ar); 128.54 (Ar); 128.12 (Ar); 127.29 (C5); 126.77 (Ar); 125.64 (Ar); 123.06 (Ar); 115.69 (C13); 110.39 (Cp); 50.84 (C4); 41.60 (C7); 20.10 (C14). **HMBC** (300 MHz, C_6D_6, selected data only) δ 5.55 (Cp) ↔ δ 110.39 (Cp); δ 4.93, 4.90 (=CH_2) ↔ δ 163.66 (C3), 140.94 (C12), 20.10 (C14); δ 3.33 (–CH_2–Ph) ↔ δ 187.87 (C6), 143.60 (–CH_2–Ph *ipso*), 127.29 (C5), 50.84 (C4); δ 3.49 (H4) ↔ δ 187.87 (C6), 163.66 (C3), 127.29 (C5), 41.60 (–CH_2–Ph); δ 1.74 (CH_3) ↔ δ 163.66 (C3), 140.94 (C12), 115.69 (C13). **HRMS** for $C_{30}H_{29}NTi$ requires *m/z* 451.17795, found 451.17871.

1,1–Bis(cyclopentadienyl)–5–benzyl–3–isopropenyl–6–phenyltitanacyclo–2–azahexa–3,5–diene 231.

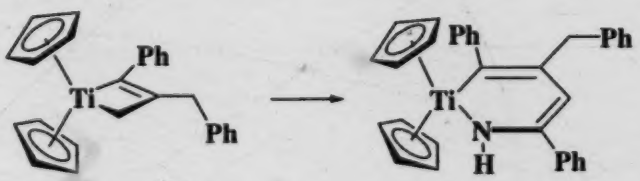


231

A solution of **230** in C_6D_6 was left to stand at room temperature for ca. 7 days, after which it had changed quantitatively to 1,1–bis(cyclopentadienyl)–5–benzyl–3–isopropenyl–6–phenyltitanacyclo–1–azahexa–3,4–diene **231**. Spectroscopic data for **231**: **^{1}H NMR** (360 MHz, C_6D_6) δ 7.65 (broad singlet, 1H, ArH); 7.20–7.10 (m, 4H obscured by residual C_6D_6, ArH); 7.00 (m, 3H, ArH); 6.82 (broad multiplet, 2H, ArH); 5.90 (s, 1H, H4); 5.51 (s, 10H, CpH); 4.82 (s, 1H, H13); 4.75 (s, 1H, H13'); 3.59 (broad singlet, 2H,

H7); 1.85 (s, 3H, H14). **^{13}C APT NMR** (100 MHz, C_6D_6, assignments confirmed by HMQC and HMBC spectra) δ 230.14; 155.41; 154.99; 144.25 (C12); 143.58 (C8); 137.77 (C5); 129.27; 128.34 (C9); 126.88; 125.57; 123.65; 115.56 (C4); 112.33 (C13); 110.38 (Cp); 43.83 (C7); 20.69 (C14). **HMQC** (600 MHz, C_6D_6, selected data only) δ 7.20 ↔ δ 125.57; δ 7.10 ↔ δ 123.65; δ 6.82 ↔ δ 126.88; δ 5.90 (H4)↔ δ 115.56 (C4); δ 5.51 (Cp<u>H</u>)↔ δ 110.38 (Cp); δ 4.82 (H13)↔ δ 112.33 (C13); δ 4.75 (H13') ↔ δ 112.33 (C13); δ 3.59 (H7) ↔ δ 43.83 (C7); δ 1.85 (H14) ↔ δ 20.69 (C14). **HMBC** (600 MHz, C_6D_6, selected data only) δ 7.15 (H16) ↔ δ 154.99 (C3); δ 5.90 (H4)↔ δ 144.25 (C12), 43.84 (C7), 20.69 (C14); δ 4.82 (H13) ↔ δ 154.99 (C3), 20.69 (C14); δ 4.75 (H13') ↔ δ 154.99 (C3), 20.69 (C14); δ 3.59 (H7) ↔ δ 143.58 (C8), 137.77 (C5), 128.34 (C9), 115.56 (C4); δ 1.85 (H14) ↔ δ 154.99 (C3), 144.25 (C12), 112.33 (C13). HRMS for $C_{30}H_{29}NTi$ requires *m/z* 451.17795, found 451.17843.

1,1–Bis(cyclopentadienyl)–5–benzyl–3,6–diphenyltitanacyclo–2–azahexa–3,5–diene 234.



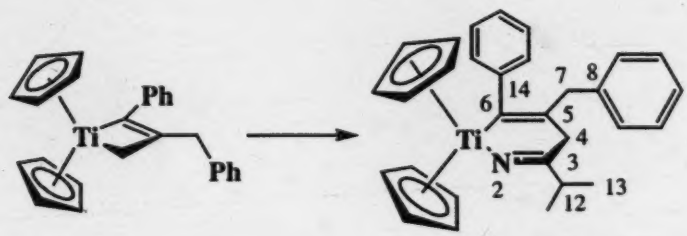
234

To a solution of 1,1–bis(cyclopentadienyl)–3–benzyl–2–phenyltitanacyclobutene **107** (10 mg, 0.026 mmol) in toluene at room temperature was added four equivalents of

benzonitrile (10.7 mg, 0.10 mmol). The solution was stirred for five hours at room temperature during which time the colour of the solution turned from red to brown–red. The solvent was removed in vacuo, and the residue was triturated with pentane and was filtered through a short column of celite followed by concentration to reveal 1,1–bis(cyclopentadienyl)–5–benzyl–3,4,7–triphenyltitanacycloocta–2,8–diaza–2,4,7–triene **233** (*vide infra*) in 97% yield. Left in a sealed NMR tube in perdeuterobenzene, the compound **233** extruded one equivalent of benzonitrile and converted (quantitatively by ^{1}H NMR spectroscopy) into 1,1–bis(cyclopentadienyl)–5–benzyl–3,6–diphenyltitanacyclohexa–2–aza–3,5–diene **234**. Spectroscopic data for **234**: **FTIR** (cast, C_6D_6, selected data only) 3341 cm^{-1} (sharp, medium). **^{1}H NMR** (500 MHz, C_6D_6) δ 7.52 (s, 1H, Ar<u>H</u>); 7.31 (doublet of multiplets, J_{HH} = 6.8 Hz, 2H, ArH); 7.18–7.08 (multiplet, 12H, partially obscured by residual C_6H_6); 6.98 (m, 3H, ArH); 6.78 (d, 2H, J_{HH} = 6.8 Hz); 6.10 (d, J_{HH} = 1.2 Hz , 1H); 5.53 (s, 22H, tBuCp); 3.64 (s, 2H). **^{1}H NMR GCOSY** (500 MHz, C_6D_6, selected data only) δ 7.52 (ArH) ↔ 6.10 (H4); δ 7.2 ↔ 6.8, 3.6. **^{13}C (APT) NMR** (125 MHz, C_6D_6, assignments confirmed by HMQC, and HMBC spectra) δ 156.54 (C3); 154.98 (C16); 143.52 (C8); 142.33 (C12); 138.46 (C5); 129.31 (Ar); 128.81 (Ar); 128.39 (C9); 128.33 (C14); 126.99 (C18); 126.60 (Ar); 125.62 (C13); 123.70 (Ar); 114.88 (C4); 110; 43.97 (C7). **HMQC** (500 MHz, C_6D_6, selected data only) δ 6.11 (H4) ↔ δ 114.88 (C4); δ 3.65 (H7) ↔ δ 43.97 (C7). **HMBC** (500 MHz, C_6D_6, selected data only) δ 7.31 (H13) ↔ δ 156.54 (C3), 128.33 (C14), 125.62 (C13); δ 7.18 (H18) ↔ δ 154.98 (C16), 126.99 (C18); δ 7.14 (H10) ↔ δ 143.52 (C8); δ 6.99 (Ar<u>H</u>) ↔ δ 126.60 (Ar); δ 6.11 (H4) ↔ δ 231 (C6), 156.54 (C3), 142.33 (C12), 43.97 (C7); δ 3.61 (H7) ↔ δ

231 (C6), 143.52 (C8), 138.46 (C5), 128.39 (C9), 114.88 (C4). **HRMS** for $C_{33}H_{29}NTi$ requires *m/z* 487.17795, found m/z 487.17969.

1,1–Bis(cyclopentadienyl)–5–benzyl–3–isopropyl–6–phenyltitanacyclo–2–aza–2,5–diene 228.

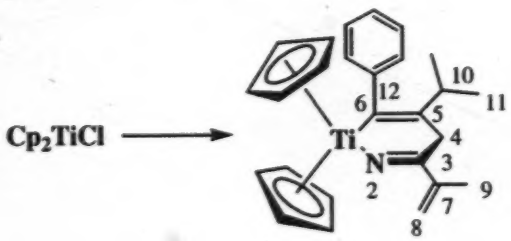


228

To a solution of 1,1–bis(cyclopentadienyl)–3–benzyl–2–phenyltitanacyclobutene **107** (10 mg, 0.026 mmol) in toluene at room temperature in a thick–walled glass reaction vessel with removable Teflon© stopcock was added isobutyronitrile (7.2 mg, 0.10 mmol). The solution was stirred for four hours at 50 °C during which time the colour of the solution turned from red to brown–red. Evaporation of solvent under reduced pressure followed by recrystallization from hexane at –35 °C gave unstable 1,1–bis(cyclopentadienyl)–5–benzyl–3–isopropyl–6–phenyltitanacyclo–2–azahexa–2,5–diene **228** (10.2 mg, 85%) as a spectroscopically clean dark–red powder. Spectroscopic data for **228**: **^{1}H NMR** (360 MHz, C_6D_6) δ 7.19 (m, 6H, Ar<u>H</u>); 7.15 (m, partially obscured by residual C_6H_6, 2H, Ar<u>H</u>); 7.05 (m, 1H, Ar<u>H</u>); 6.96 (tt, $^3J_{HH}$=7.2 Hz, $^4J_{HH}$=1.3 Hz, 1H, H17); 5.57 (s, 10H, Cp); 3.33 (s, 2H, H7); 3.11 (s, 2H, H4); 1.74 (septet, $^3J_{HH}$ = 6.8 Hz, 1H, H12); 0.83 (d, $^3J_{HH}$ = 6.8 Hz, 6H, H13). **^{13}C (APT) NMR** (75 MHz, C_6D_6, assignments confirmed by

HMBC spectrum) δ 188.36 (C6); 171.36 (C3); 155.14 (C14); 143.67 (C8); 131.92 (Ar); 128.69 (Ar); 128.53 (C10); 128.15 (C9); 126.71 (C5); 125.65 (Ar); 123.01 (Ar); 110.39 (Cp); 53.85 (C4); 41.40 (C7); 35.26 (C12); 20.07 (C13). **HMBC** (300 MHz, C_6D_6, selected data only) δ 7.19 (H9) ↔ δ 143.67 (C8), 128.53 (C10), 126.71 (C5), 41.40 (C7); δ 7.18 (H15) ↔ δ 155.14 (C14); δ 3.33 (H7) ↔ δ 188.36 (C6), 143.67 (C8), 128.15 (C9), 126.71 (C5), 53.85 (C4); δ 3.11 (H4) ↔ δ 188.36 (C6), 171.36 (C3), 126.71 (C5), 41.40 (C7); δ 0.83 (H13) ↔ δ 171.36 (C3), 35.26 (C12), 20.07 (C13). **HRMS** for $C_{30}H_{32}NTi$ requires *m/z* 454.20142, found 454.20085.

1,1–Bis(cyclopentadienyl)–3–isopropenyl–5–isopropyl–6–phenyltitanacyclo–2–azahexa–2,5–diene 232.

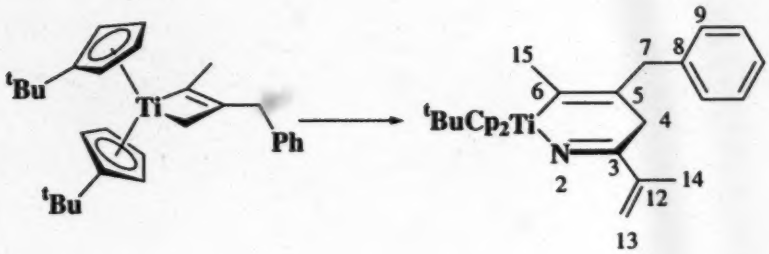


232

To a solution of 1,1–bis(cyclopentadienyl)–3–isopropyl–2–phenyltitanacyclobutene (5.0 mg, 0.015 mmol) in toluene at room temperature was added isopropenyl nitrile (1.1 mg, 0.016 mmol). The solution was stirred at room temperature for 16 hours, after which time the solvent was removed in vacuo. The solvent was removed *in vacuo*, and the

residue was triturated with pentane and was filtered through a short column of celite followed by concentration to yield the product **232** as a spectroscopically clean red solid, in quantitative yield. Spectroscopic data for 1,1–bis(cyclopentadienyl)–3–isopropenyl–5–isopropyl–6–phenyltitanacyclo–2–azahexa–2,5–diene **232**: **^{1}H NMR** (360 MHz, C_6D_6) δ 7.23 (dd, $^3J_{HH}$ = 7.9 Hz, $^3J_{HH}$ = 7.5 Hz, 2H, ArH *meta*); 7.02–6.97 (m, 3H, ArH); 5.53 (s, 10H, CpH); 5.23 (s, 1H, H8); 5.10 (t, J_{HH} = 1.3 Hz, H8'); 3.54 (s, 2H, H4); 2.70 (septet, $^3J_{HH}$ = 6.9 Hz, 1H, H10); 1.82 (s, 3H, H9); 0.95 (d, $^3J_{HH}$ = 6.9 Hz, 6H, H11). **^{13}C (APT) NMR** (75 MHz, C_6D_6, assignments confirmed by HMQC and HMBC spectra) δ 226.21 (C6); 163.65 (C3); 155.58 (Ar *ipso*); 141.59 (C7); 133.63 (C5); 128.53 (Ar); 126.48 (Ar); 122.74 (Ar); 115.32 (C8); 110.42 (Cp); 44.13 (C4); 32.80 (C10); 22.79 (C11); 20.32 (C9). **HMQC** (300 MHz, C_6D_6, decoupled, selected data only) δ 7.00 (ArH) ↔ δ 126.48 (Ar); δ 6.97 (ArH) ↔ δ 122.74 (Ar); δ 5.23 (H8) (δ 115.32 (C8); δ 5.10 (H8') ↔ δ 115.32 (C8); δ 3.54 (H4) ↔ δ 44.13 (C4); δ 1.82 (H9) ↔ δ 20.32 (C9); δ 0.95 (H11) ↔ δ 22.79 (C11). **HMBC** (300 MHz, C_6D_6, selected data only) δ 5.23 (H8) ↔ δ 163.65 (C3); δ 3.54 (H4) ↔ δ 163.65 (C3), 133.63 (C5), 32.80 (C10); δ 2.70 (H10) ↔ δ 20.79 (C11); δ 1.82 (H9) ↔ δ 163.65 (C3), 141.59 (C7), 115.32 (C8); δ 0.95 (H11) ↔ δ 133.63 (C5), 22.79 (C11), 20.32 (C9). **HRMS** for $C_{26}H_{29}NTi$ requires *m/z* 403.17795, found *m/z* 403.17815.

1,1–Bis(*tert*–butylcyclopentadienyl)–5–benzyl–3–isopropenyl–6–methyltitanacyclo–2–azahexa–2,5–diene 235.

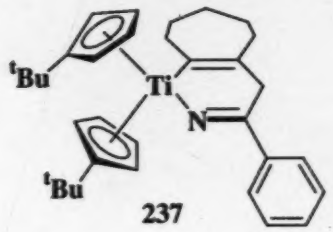


235

To a room temperature solution of 1,1–bis(*tert*–butylcyclopentadienyl)–3–benzyl–1–methyltitanacyclobutadiene (7 mg, 0.016 mmol) in dry toluene in a thick–walled glass reaction vessel with removable Teflon© stopcock was added isopropenylnitrile (5.4 mg, 0.080 mmol). The solution was heated at 50°C for 16 hours then the reaction solution was cooled to room temperature and solvents removed *in vacuo*. Product 1,1–bis(*tert*–butylcyclopentadienyl)–5–benzyl–3–isopropenyl–6–methyltitanacyclo–2–azahexa–2,5–diene was isolated as a brown solid (5.9 mg, 74% yield). Spectroscopic data for **235**: **^{1}H NMR** (360 MHz, C_6D_6) δ 7.26–7.09 (m, obscured by residual C_6H_6, Ar<u>H</u>); 5.76 (m, 4H, Cp<u>H</u>); 5.53 (dd, $^3J_{HH}$ = 5.0 Hz, $^3J_{HH}$ = 2.9 Hz, 2H, Cp<u>H</u>); 5.29 (dd, $^3J_{HH}$ = 6.5 Hz, $^3J_{HH}$ = 3.0 Hz, 2H, Cp<u>H</u>); 5.09 (s, 1H, H13); 4.99 (s, 1H, H13'); 3.52 (s, 2H, H4); 3.40 (s, 2H, H7); 1.80 (s, 3H, H14); 1.68 (s, 3H, H15); 1.47 (s, 18H, [(C<u>H</u>$_3$)$_3$CCpH]). **^{13}C (APT) NMR** (75 MHz, C_6D_6, selected data only) δ 181.77 (C6); 165.70 (C3); 150.98 ; 142.85; 142.63; 141.54 (C8); 141.31 (C12); 138.98 ([(CH$_3$)$_3$CCp] *ipso*); 128.65 (Ar); 126.70 (Ar); 126.12 (C5); 125.54 (C10); 116.48 (C13); 112.63 ([(CH$_3$)$_3$C<u>C</u>p]); 111.32

([(CH$_3$)$_3$C<u>C</u>p]); 110.78 ([(CH$_3$)$_3$C<u>C</u>p]); 106.65 ([(CH$_3$)$_3$C<u>C</u>p]); 103.44 ([(CH$_3$)$_3$C<u>C</u>p]); 53.93 (C4); 42.56 ([(CH$_3$)$_3$<u>C</u>Cp]); 38.34 (C7); 31.66 ([(<u>C</u>H$_3$)$_3$CCp]); 31.27 ([(CH$_3$)$_3$<u>C</u>Cp']); 25.18 (C15); 20.68 (C14). **HMQC** (300 MHz, decoupled, C_6D_6, selected data only) δ 7.09 (Ar<u>H</u>) ↔ δ 125.55 (C10); δ 5.76 (Cp<u>H</u>) ↔ δ 112.63 ([(CH$_3$)$_3$C<u>C</u>p]), 110.78 ([(CH$_3$)$_3$C<u>C</u>p]); δ 5.53 (Cp<u>H</u>) ↔ δ 106.65 ([(CH$_3$)$_3$C<u>C</u>p]); δ 5.29 (Cp<u>H</u>) ↔ δ 103.44 ([(CH$_3$)$_3$C<u>C</u>p]); δ 5.09 (H13) ↔ δ 116.48 (C13); δ 4.99 (H13') ↔ δ 116.48 (C13); δ 3.52 (H4) ↔ δ 53.93 (C4); δ 3.40 (H7) ↔ δ 38.34 (C7); δ 1.80 (H14) ↔ δ 20.68 (C14); δ 1.68 (H15) ↔ 25.18 (C15); δ 1.47 ([(CH$_3$)$_3$CCpH]) ↔ 31.66 ([(CH$_3$)$_3$CCp]). **HMBC** (300 MHz, C_6D_6, selected data only) δ 7.22 (H9) ↔ 141.54 (C8), 125.55 (C10), 38.34 (C7); δ 5.76 (CpH) ↔ 138.98 ([(CH$_3$)$_3$CCp] ipso), 106.65 ([(CH$_3$)$_3$CCp]), 103.44 ([(CH$_3$)$_3$CCp]); δ 5.53 (CpH) ↔ 110.78 ([(CH$_3$)$_3$CCp]), 103.44 ([(CH$_3$)$_3$CCp]); δ 5.09 (H13) ↔ 165.70 (C3), 20.68 (C14); δ 4.99 (H13) ↔ 165.70 (C3), 20.68 (C14); δ 3.52 (H4) ↔ 181.77 (C6), 165.70 (C3), 126.12 (C5); δ 3.40 (H7) ↔ 181.77 (C6), 141.54 (C8), 126.12 (C5), 3.93 (C4); δ 1.80 (H14) ↔ δ 165.70 (C3), 141.31 (C12), 116.48 (C13); δ 1.68 (H15) ↔ δ 181.77 (C6), 126.12 (C5); δ 1.47 ([(C<u>H</u>$_3$)$_3$CCpH]) ↔ δ 138.98 ([(CH$_3$)$_3$CCp] *ipso*), 31.66 ([(<u>C</u>H$_3$)$_3$CCp]), 31.27 ([(CH$_3$)$_3$<u>C</u>Cp']). **HRMS** for $C_{33}H_{43}NTi$ requires *m/z* 501.28751, found *m/z* 501.28764.

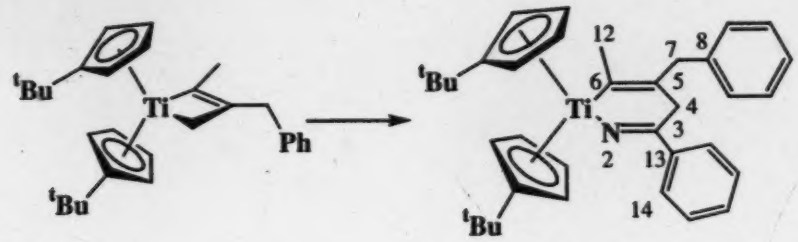
8,8–Bis(*tert*–butylcyclopentadienyl)titanabicyclo[5.4.0]–9–aza–10–phenylundeca–1–(7)–9–(10)diene 237.



237

A toluene solution of 8,8–bis(*tert*–butylcyclopentadienyl)titanabicyclo[5.2.0]nona–1–(7)–ene[28] (58 mg, 0.146 mmol), was treated with benzonitrile (30.2 mg, 0.293 mmol), and the solution heated to 60 °C at which it was maintained for six hours. The solvent was removed *in vacuo*, and the residue was triturated with pentane and was filtered through a short column of celite followed by concentration to yield product **237** in 56% yield. Spectroscopic data for **237**: **^{1}H NMR** (360 MHz, C_6D_6) δ 7.59 (d, J = 7.3 Hz, 2H); 7.18–7.10 (m, obscured by residual C_6H_6); 5.90 (s, 2H); 5.84 (s, 2H); 5.61 (s, 2H); 5.35 (s, 2H); 3.74 (s, 2H); 2.20 (m, 2H); 2.00 (m, 2H); 1.82 (broad singlet, 2H); 1.65 (broad singlet, 2H); 1.52 (broad singlet, 2H); 1.13 (s, 18H). **^{13}C APT NMR** (75 MHz, C_6D_6) δ 188.4; 163.0; 139.2; 136.1; 130.7; 129.2; 111.5; 109.4; 105.9; 104.3; 57.3; 39.0; 34.0; 33.2; 32.6; 31.4; 27.1.

1,1–Bis(*tert*–butylcyclopentadienyl)–5–benzyl–6–methyl–3–phenyltitanacyclo–2–azahexa–2,5–diene 238.

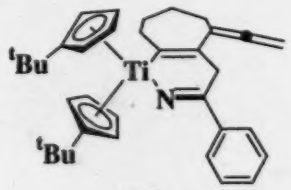


238

A solution of 1,1–bis(*tert*–butylcyclopentadienyl)–3–benzyl–1–methyltitanacyclobutene (5.0 mg, 0.011 mmol) in toluene at room temperature was added to a thick–walled glass reaction vessel with removable Teflon© stopcock. Benzonitrile (1.4 mg, 0.014 mmol) at room temperature was added to the solution and the solution was stirred at 50 °C for 48 hours. The solvent was removed *in vacuo*, and the residue was triturated with pentane and was filtered through a short column of celite followed by concentration to yield product **238** as a brown solid, in 82% yield. Spectroscopic data for **238**: **^{1}H NMR** (360 MHz, C_6D_6) δ 7.51 (dt, $^3J_{HH}$ = 6.8 Hz, $^3J_{HH}$ = 1.5 Hz, 2H, H14); 7.29 (m, 6H, ArH); 7.12 (m, 2H, obscured by residual C_6H_6, ArH); 5.80 (m, 4H, [$(CH_3)_3CCpH$]); 5.60 (dd, $^3J_{HH}$ = 5.2 Hz, $^3J_{HH}$ = 2.2 Hz, 2H, [$(CH_3)_3CCpH$]); 5.34 (dd, $^3J_{HH}$ = 5.3 Hz, $^3J_{HH}$ = 3.0 Hz, 2H, [$(CH_3)_3CCpH$]); 3.77 (broad singlet, 2H, H4); 3.48 (s, 2H, H7); 1.72 (s, 3H, H12); 1.08 (s, 18H, [$(CH_3)_3CCpH$]). **^{13}C APT NMR** (125 MHz, C_6D_6, assignments confirmed by GCOSY, HMQC and HMBC spectra) δ 182.33 (C6); 163.18 (C3); 142.89 (C8); 139.62 (C13); 129.28 (Ar); 128.77 (Ar); 128.65 (Ar); 128.33 (Ar); 127.76 (Ar); 125.86 (C5);

111.93 ([$(CH_3)_3CCp$]); 110.66 ([$(CH_3)_3CCp$]); 106.13 ([$(CH_3)_3CCp$]); 103.96 ([$(CH_3)_3CCp$]); 54.28 (C4); 38.48 (C7); 32.73 ([$(CH_3)_3CCp$]); 31.38 ([$(CH_3)_3CCp$]); 25.09 (C12). **GCOSY** (500 MHz, C_6D_6, selected correlations only) δ 3.77 (H4) ↔ δ 1.72 (H12). **HMQC** (300 MHz, C_6D_6, decoupled, selected data only) δ 3.77 (H4) ↔ δ 54.22 (C4); δ 3.48 (H7) ↔ δ 38.41 (C7); δ 1.72 (H12) ↔ δ 25.03 (C12); δ 1.08 ([$(C\underline{H}_3)_3CCpH$]) ↔ δ 31.32 ([$(\underline{C}H_3)_3CCp$]). **HMBC** (300 MHz, C_6D_6, selected data only) δ 7.51 (H14) ↔ δ 163.13 (C3); δ 7.14 ↔ δ 136.11 (); δ 3.77 (H4) ↔ δ 182.28 (C6), 163.13 (C3), 125.79 (C5); 3.48 (H7) ↔ δ 182.28 (C6), 142.84 (C8), 125.79 (C5), 54.22 (C4); δ 1.72 (H12) ↔ δ 182.28 (C6), 125.79 (C5). **HRMS** for $C_{36}H_{43}NTi$ requires *m/z* 537.28748, found *m/z* 537.28818.

8,8–Bis(*tert*–butylcyclopentadienyl)titanabicyclo[5.4.0]–2–allenyl–9–aza–10–phenyl–undeca–1–(7)–9(10)–diene 239.

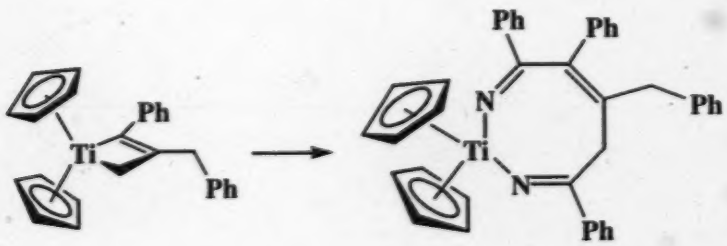


239

To a room temperature solution of 8,8–bis(*tert*–butylcyclopentadienyl)titanabicyclo[5.2.0]–2–allenyl–non–1–(7)–ene **180** (50 mg, 0.118 mmol) in dry toluene was added benzonitrile (121.6 mg, 1.18 mmol). The solution was stirred at room temperature for four hours then the solvents removed *in vacuo*. The impure product was isolated as a red solid (55 mg, 89% yield). Spectroscopic data for

crude product: **^{1}H NMR** (500 MHz, C_6D_6) δ 7.64 (doublet of multiplets, J_{HH} = 7.0 Hz, 1H); 7.2 – 7.0 (m, partially obscured by residual C_6H_6); 5.87 (apparent quartet, J_{HH} = 3.1 Hz, 1H); 5.86 (apparent quartet, J_{HH} = 2.3 Hz, 1H); 5.77 (apparent quartet, J_{HH} = 3.1 Hz, 1H); 5.61 (apparent quartet, J_{HH} = 3.1 Hz, 1H); 5.59 (apparent quartet, J_{HH} = 2.3 Hz, 1H); 5.56 (apparent quartet, J_{HH} = 2.3 Hz, 1H); 5.44 (apparent quartet, J_{HH} = 3.1 Hz, 1H); 5.30 (apparent quartet, J_{HH} = 2.9 Hz, 1H); 4.86 (s, 1H); 4.74 (s, 1H); 4.13 (s, 1H); 3.28 (s, 1H); 2.59 (broad singlet, 1H); 2.39 (broad singlet, 1H); 2.33 (multiplet, 1H); 2.07 (multiplet, 1H); 1.84 (multiplet, 2H); 1.70 (multiplet, 2H); 1.13 (s, 5H); 1.11 (s, 5H). **^{13}C NMR APT** (125 MHz, C_6D_6) δ 162.84; 139.59; 139.14; 135.78; 129.02;128.25; 125.37; 111.71; 111.02; 110.71; 109.81; 109.15; 107.55; 106.64; 106.18; 103.80; 73.14; 71.26; 55.34; 37.88; 36.76; 32.44; 32.21; 31.33; 31.18; 28.59; 27.97. **HRMS** for $C_{35}H_{43}NTi$ requires *m/z* 525.28748, found *m/z* 525.28774.

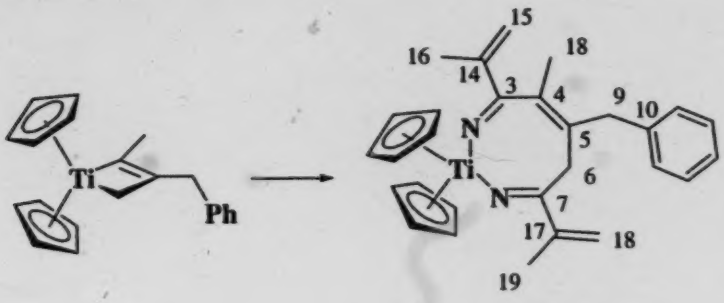
1,1–Bis(cyclopentadienyl)–5–benzyl–3,4,7–triphenyltitanacyclo–2,8–diazaocta–2,4,7–triene 233.



233

To a solution of 1,1–bis(cyclopentadienyl)–3–benzyl–2–phenyltitanacyclobutene (10 mg, 0.026 mmol) in toluene at room temperature was added benzonitrile (10.7 mg, 0.104 mmol). The solution was stirred for five hours at room temperature during which time the colour of the solution turned from red to brown–red. Evaporation of solvent under reduced pressure followed by recrystallization from hexane at –35 °C gave unstable 1,1–bis(cyclopentadienyl)–5–benzyl–3,4,7–triphenyltitanacyclo–2,8–diazaocta–2,4,7–triene, **233** (14.9 mg, 97%) as a brown powder. The compound undergoes a colour change in solution (C_6D_6) at room temperature over a 12 hour period from deep red to deep green. One equivalent of benzonitrile is lost and the compound isomerizes to the more stable 1,1–bis(cyclopentadienyl)–5–benzyl–3,6–diphenyltitanacyclo–2–azacyclohexa–3,5–diene **234** (*vide supra*). Spectroscopic data for **233**: **^{1}H NMR** (360 MHz, C_6D_6) δ 7.47 (m, 2H, Ar<u>H</u>); 7.21 (m, 8H, Ar<u>H</u>); 7.15–6.90 (m, 10H, Ar<u>H</u>); 5.60 (s, 10H, <u>Cp</u>); 3.70 (s, 2H,); 3.38 (s, 2H,). **^{13}C APT NMR** (125 MHz, C_6D_6) δ 188.4; 161.3; 156.5; 154.9; 154.8; 143.6; 143.6; 136.2; 131.9; 129.4; 129.3; 128.8; 128.8; 128.6; 128.5; 128.4; 128.3; 127.1; 126.9; 126.8; 126.6; 125.7; 125.6; 123.7; 123.1; 114.8; 110.6; 51.5; 43.9; 41.6. **HMBC** (300 MHz, C_6D_6, selected data only) δ 3.70 ↔ δ 188.4, 161.3, 127; δ 3.38 ↔ δ 188.4, 143.6, 128, 127, 51.5. **HRMS** $C_{40}H_{34}N_2Ti$ not observed. $C_{33}H_{29}NTi$ requires *m/z* 487.17795, found *m/z* 487.17893.

1,1–Bis(cyclopentadienyl)–5–benzyl–3,7–bis(isopropenyl)–4–methyltitanacyclo–2,8–diazaocta–2,4,7–triene 240.

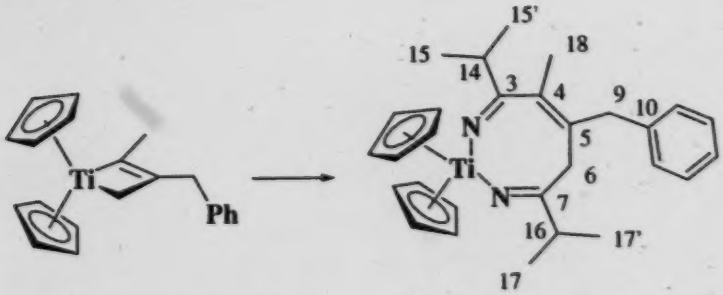


240

To a solution of 1,1–bis(cyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene 16 (10 mg, 0.031 mmol) in toluene at room temperature in a thick–walled glass reaction vessel with removable Teflon© stopcock was added isopropenylnitrile (8.3 mg, 0.124 mmol). The solution was stirred at 40 °C for 16 hours during which time the red solution turned dark red. Evaporation of solvent under reduced pressure gave 1,1–bis(cyclopentadienyl)–5–benzyl–3,7–bis(isopropyl)–4–methyltitanacyclo–1,8–diazaocta–2,4,6–triene **240** (14 mg, 99%) as a spectroscopically clean red oil. Spectroscopic data for **240**: **^{1}H NMR** (500 MHz, C_6D_6) δ 7.5–7.4 (m, 5H, ArH); 5.65 (s, 20H, CpH); 5.27 (m, 1H, H18); 5.22 (m, 1H, H15); 5.13 (m, 1H, H18'); 5.11 (m, 1H, H15); 3.56 (d, [A of AB quartet], $^2J_{HH}$ = 15.5 Hz, 1H, H9); 3.30 (d, [A of AB quartet], $^2J_{HH}$ = 11.5 Hz, 1H, H6); 3.24 (d, [B of AB quartet], $^2J_{HH}$ = 15.5 Hz, 1H, H9'); 3.12 (d, [B of AB quartet], $^2J_{HH}$ = 11.5 Hz, 1H, H6'); 1.86 (s, 3H, H16); 1.82 (s, 3H, H20); 1.80 (s, 3H, H19). **^{13}C APT NMR** (75 MHz, C_6D_6, assignments confirmed by HMBC spectrum) δ 168.23 (C3); 160.55 (C7); 145.04 (C17);

143.98 (C14); 140.12 (C10); 137.20; 133.10; 128.52; 128.47; 126.06; 114.38 (C15); 114.06 (C18); 111.21; 110.13 (Cp); 109.51; 105.91; 39.39 (C9); 37.44 (C6); 20.60 (C19); 20.15 (C16); 17.91 (C20). **HMBC** (300 MHz, C_6D_6, selected data only) δ 5.27 (H15) ↔ δ 20.15 (C16); δ 5.22 (H15') ↔ δ 168.23 (C3), 20.15 (C16); δ 5.13 (H19) ↔ δ 160.55 (C7), 20.60 (C20); δ 5.11 (H19') ↔ δ 160.55 (C7), 20.60 (C20); δ 3.56 (H9) ↔ δ 140.12 (C10), 137.20, 133.10, 39.39 (C9); δ 3.30 (H6) ↔ δ 160.55 (C7), 137.20, 133.10, 37.44 (C6); δ 3.24 (H9') ↔ δ 140.12 (C10), 137.20, 133.10, 39.39 (C9); δ 3.30 (H6') ↔ δ 160.55 (C7), 145.04 (C17), 137.20, 133.10, 37.44 (C6); δ 1.86 (H16) ↔ δ 168.23 (C3), 143.98 (C14), 114.38 (C15); δ 1.82 (H20) ↔ δ 168.23 (C3), 137.20, 133.10; δ 1.80 (H19) ↔ δ 145.04 (C17), 114.06 (C18). **HRMS** $C_{29}H_{33}N_2Ti$ not observed. Parent *m/z* + H: for $C_{29}H_{33}N_2Ti$ requires *m/z* 457.21231, found *m/z* 457.21131.

1,1–Bis(cyclopentadienyl)–5–benzyl–4–methyl–3,7–bis(isopropyl)– titanacyclo–2,8–diazaocta–2,4,7–triene 241.

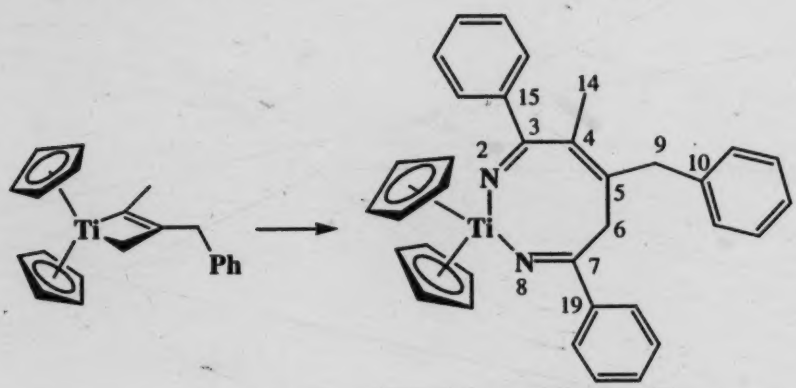


241

To a solution of 1,1–bis(cyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene (10 mg, 0.031 mmol) in toluene at room temperature in a thick–walled glass reaction vessel with

removable Teflon© stopcock was added isobutyronitrile (32 mg, 0.465 mmol). The solution was stirred at 50°C for 16h during which time the red solution turned dark red and depositing an unidentified insoluble precipitate on the side of the flask. Evaporation of solvent under reduced pressure gave 1,1–Bis(cyclopentadienyl)–5–benzyl–3,7–bis(isopropyl)–4–methyltitanacyclo–1,8–diazaocta–2,4,6–triene **241** (11 mg, 77%) as a spectroscopically clean red oil. Spectroscopic data for **241**: **^{1}H NMR** (500 MHz, C_6D_6) δ 7.25–6.9 (m, obscured by residual C_6H_6, Ar<u>H</u>); 6.65 (s, 1H, H6); 6.3–5.6 (very broad, Cp<u>H</u>); 3.76 (s, 2H, H9); 3.16 (septet, $^3J_{HH}$ = 6.6 Hz, 1H, H14); 2.99 (septet, $^3J_{HH}$ = 6.9 Hz, 1H, H16); 1.93 (s, 3H, H18); 1.37 (d, $^3J_{HH}$ = 6.6 Hz, 6H, H15); 1.34 (d, $^3J_{HH}$ = 6.9 Hz, 6H, H17). **^{13}C APT NMR** (125 MHz, C_6D_6, assignments confirmed by HMQC and HMBC spectra) δ 164.04 (C3); 163.63 (C7); 147.64 (C5); 139.74 (C10); 128.94 (Ar); 128.82 (Ar); 126.46 (Ar); 125.63 (C4); 119.82 (C6); 110.05 (Cp); 40.05 (C9); 36.30 (C16); 31.91 (C14); 22.94 (C17); 22.33 (C15); 13.53 (C18). **HMQC** (500 MHz, C_6D_6, selected data only) δ 6.65 (H6) ↔ δ 119.82 (C6); δ 3.76 (H9) ↔ δ 40.05 (C9); δ 3.16 (H14) ↔ δ 31.91 (C14); δ 2.99 (H16)↔ δ 36.30 (C16); δ 1.93 (H18) ↔ δ 13.52 (C18); δ 1.37 (H15)↔ δ 22.33 (C15); δ 1.34 (H17) ↔ δ 22.94 (C17). **HMBC** (500 MHz, C_6D_6, selected data only) δ 6.65 (H6) ↔ δ 163.63 (C7), 125.63 (C4), 40.05 (C9), 36.30 (C16); δ 3.76 (H9) ↔ δ 147.64 (C5), 139.74 (C10), 128 (C11), 125.63 (C4), 119.82 (C6); δ 3.16 (H14) ↔ δ 164.04 (C3), 22.33 (C15); δ 2.99 (H10) ↔ δ 163.63 (C7), 22.94 (C17); δ 1.93 (H18) ↔ δ 164.04 (C3), 147.64 (C5), 125.63 (C4), 13.53 (self–correlation); δ 1.37 (H15) ↔ δ 164.04 (C3), 31.91 (C14), 22.33 (C15); δ 1.34 (H17) ↔ δ 163.63 (C7), 36.30 (C16), 22.94 (C17). **HRMS** for $C_{29}H_{36}N_2Ti$ requires *m/z* 460.23581, found *m/z* 460.23583.

1,1–Bis(cyclopentadienyl)–5–benzyl–4–methyl–3,7–diphenyltitanacyclo–2,8–diazaocta–2,4,7–triene 242.



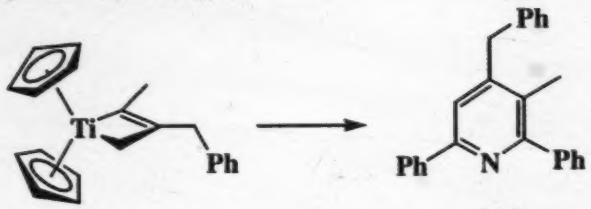
242

To a solution of 1,1–bis(cyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene (100 mg, 0.310 mmol) in toluene at room temperature in a thick–walled glass reaction vessel with removable Teflon© stopcock was added benzonitrile (64 mg, 0.620 mmol). The solution was stirred at 50 °C for 7h during which time the red solution turned dark red. Evaporation of solvent under reduced pressure gave 1,1–Bis(cyclopentadienyl)–5–benzyl–4–methyl–3,7–bisphenyltitanacyclo–2,8–diazaocta–2,4,7–triene **242** (63 mg, 87%) as a spectroscopically clean red solid. Spectroscopic data for **242** : **^{1}H NMR** (360 MHz, C_6D_6) δ 7.61 (m, J_{HH} = 9 Hz, 4H, H16,16', 20,20'); 7.32–7.13 (m, 11H, obscured by residual C_6H_6, Ar<u>H</u>); 5.79 (s, 5H, Cp<u>H</u>); 5.69 (s, 5H, Cp<u>H</u>); 3.60 (d, $^2J_{HH}$ = 11.3 Hz, 1H, H6); 3.52 (d, $^2J_{HH}$ = 15.6 Hz, 1H, H9); 3.45 (d, $^2J_{HH}$ = 11.3 Hz, 1H, H6'); 3.08 (d, $^2J_{HH}$ = 15.6 Hz, 1H, H9'); 1.79 (s, 3H, H14). **^{13}C APT NMR** (75 MHz, C_6D_6, assignments

confirmed by HMQC and HMBC spectra) δ 165.98 (C3); 157.82 (C7); 140.21 (Ar *ipso*); 140.06 (Ar *ipso*); 139.61 (C10); 136.69 (either C4 or C5); 135.40 (either C4 or C5); 128.79 (Ar); 128.75 (Ar); 128.52 (Ar); 127.50 (Ar); 126.41(Ar); 111.48 (Cp); 110.32 (Cp); 109.90 (Cp); 40.67 (C6); 38.08 (C9); 17.96 (C14). **HMQC** (300 MHz, C_6D_6, selected data only) δ 3.60 (H6) ↔ δ 40.67 (C6); δ 3.52 (H9) ↔ δ 38.08 (C9); δ 3.45 (H6') ↔ δ 40.67 (C6); δ 3.08 (H9') ↔ δ 38.08 (C9); δ 1.79 (H14) ↔ δ 17.96 (C14). **HMBC** (300 MHz, C_6D_6, selected data only) δ 7.61 (H16,16', 20,20') ↔ δ 165.98 (C3), 157.82 (C7); δ 3.60 (H6) ↔ δ 157.82 (C7), 136.69 (either C4 or C5), 135.40 (either C4 or C5); δ 3.52 (H9) ↔ δ 139.61 (C10), 136.69 (either C4 or C5), 135.40 (either C4 or C5), 126.41 (Ar), 40.67 (C6); δ 3.45 (H6') ↔ δ 157.82 (C7), 136.69 (either C4 or C5), 135.40 (either C4 or C5), 38.08 (C9); δ 3.08 (H9') ↔ δ 139.61 (C10), 136.69 (either C4 or C5), 135.40 (either C4 or C5), 126.41 (Ar), 40.67 (C6); δ 1.79 (H14) ↔ δ 165.98 (C3), 136.69 (either C4 or C5), 135.40 (either C4 or C5). Attempted EI–MS provides mass spectrum for $C_{28}H_{28}NTi$. Loss of one equivalent of benzonitrile (de–insertion), occurs in the ionization chamber. Only the compound containing one equivalent of benzonitrile is sufficiently stable to survive long enough to be detected. **HRMS** for $C_{28}H_{28}NTi$ requires *m/z* 426.17014, found *m/z* 426.17073.

vii. pyridine formation

4–Benzyl–3–methyl–2,6–diphenylpyridine 244.

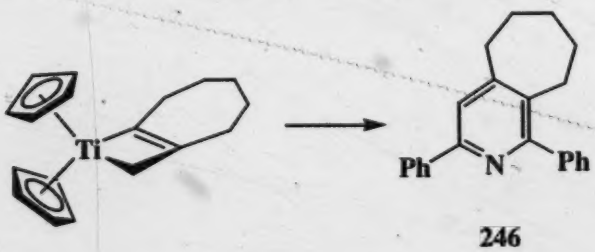


244

The general procedure for pyridine synthesis from bis(cyclopentadienyl)titanacyclobutene complexes, as illustrated for 4–benzyl–3–methyl–2,6–diphenylpyridine **244**, is as follows: to a solution of 1,1–bis(cyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene (16 mg, 0.049 mmol) in toluene at room temperature in a thick–walled glass reaction vessel with removable Teflon© stopcock, was added benzonitrile (76.8 mg, 0.745 mmol). The solution was stirred at 80 °C for two hours during which time the red solution turned brown–red. The solution was then cooled to –78 °C and anhydrous HCl gas was bubbled through the solution for approximately ten seconds. The solution was then allowed to warm to room temperature. After approximately five minutes the solution had turned bright red, indicating the formation of Cp_2TiCl_2. Evaporation of solvent under reduced pressure followed by column chromatography with neutral alumina (eluent: 10:1 CH_2Cl_2/MeOH) gave 4–benzyl–3–methyl–2,6–diphenylpyridine **244** (14.5 mg, 87%) as a spectroscopically clean yellow oil. Spectroscopic data for **244**: **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.00 (dd, $^3J_{HH}$ = 8.4 Hz,

$^4J_{HH}$ = 1.4 Hz, 2H, ArH); 7.57 (dd, $^3J_{HH}$ = 8.4 Hz, $^4J_{HH}$ = 1.4 Hz, 2H, ArH); 7.5–7.3 (m, 10H, ArH); 7.22 (m, 2H, ArH); 4.13 (s, 2H, H7); 2.27 (s, 3H, H12). **^{13}C APT NMR** (75 MHz, $CDCl_3$, assignments confirmed by GCOSY, HMQC, and HMBC spectra) δ 157.95; 153.57; 151.94; 137.87; 132.78; 132.19; 129.66; 129.35; 129.15; 128.94; 128.90; 128.69; 128.52; 128.17; 127.55; 126.82; 121.28; 40.02 (C7); 16.10 (C12). **HMQC** (600 MHz, $CDCl_3$, selected data only) δ 8.00 (ArH) ↔ δ 126.82 (Ar); δ 7.57 (ArH) ↔ δ 129.15 (Ar); δ 7.43 (ArH) ↔ δ 121.28 (Ar); δ 7.22 ↔ δ 128.52 (Ar); δ 4.13 (H7) ↔ δ 40.02 (C7); δ 2.27 (H12) ↔ δ 16.10 (C12). **HMBC** (600 MHz, $CDCl_3$, selected data only) δ 8.00 (ArH) ↔ δ 153.57 (Ar); δ 7.57 (ArH) ↔ δ 157.95 (Ar); δ 7.4 (ArH) ↔ δ 153.57 (Ar), 40.02 (C7); δ 4.13 (H7) ↔ δ 151.94 (Ar), 137.87, 129 (Ar), 121.28; δ 2.27 (H12) ↔ δ 157.95 (Ar), 151.94 (Ar), 129 (Ar). **HRMS** for $C_{25}H_{21}N$ requires *m/z* 335.16739, found *m/z* 335.16579; $C_{25}H_{20}N$ requires *m/z* 334.15958, found *m/z* 334.15967.

1,3–Diphenyl–6,7,8,9–tetrahydro–5H–cyclohepta[c]pyridine 246.



246

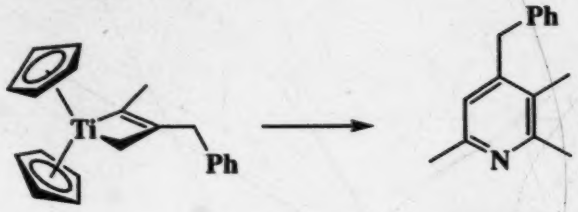
Following the general procedure described above, 8,8–bis(cyclopentadienyl)titanabicyclo[5.2.0] non–1–(7)–ene[28] (58.0 mg, 0.203 mmol) and benzonitrile (83.6 mg, 0.810 mmol) were stirred at 60 °C for 16 hours during which time the red solution turned brown. Following column chromatography with neutral alumina (eluent: petroleum ether), the product 1,3–diphenyl–6,7,8,9–tetrahydro–5H–cyclohepta[c]pyridine **246** (48.5 mg, 81%) was recovered as a spectroscopically clean yellow oil. Spectroscopic data for **246**: **^{1}H NMR** (360 MHz, C_6D_6) δ 8.04 (dm, $^3J_{HH}$ = 7.1 Hz, 2H, ArH); 7.53 (dm, $^3J_{HH}$ = 6.9 Hz, 2H, ArH); 7.50–7.33 (m, 7H, ArH); 2.92 (second order multiplet, 2H, Ar–CH_2–); 2.86 (second order multiplet, 2H, Ar–CH_2–); 1.89 (tt, $^3J_{HH}$ = 6.0 Hz, $^3J_{HH}$ = 5.7 Hz, –CH_2–CH_2–CH_2–); 1.76 (tt, $^3J_{HH}$ = 5.8 Hz, $^3J_{HH}$ = 5.2 Hz, –CH_2–CH_2–CH_2–); 1.68 (tt, $^3J_{HH}$ = 6.0Hz, $^3J_{HH}$ = 5.7 Hz, –CH_2–CH_2–CH_2–). **^{13}C (APT) NMR** (75 MHz, C_6D_6) δ 158.00; 154.21; 153.99; 141.70; 139.69; 134.97; 129.51; 128.56; 128.45; 128.01; 127.56; 126.93; 119.83; 36.73; 32.40; 30.57; 27.92; 27.66. **HRMS** for $C_{22}H_{21}N$ requires *m/z* 299.16739, found *m/z* 299.16739.

4–Isopropyl–3–methyl–2,6–diphenylpyridine 247.

247

Following the general procedure described above, 1,1–bis(cyclopentadienyl)–3–isopropyl–2–methyltitanacyclobutene (57 mg, 0.208 mmol) and benzonitrile (321.6 mg, 3.12 mmol) were stirred at 80 °C for two hours during which time the red solution turned brown–red. Following column chromatography with neutral alumina (eluent: 10:1 CH_2Cl_2/MeOH), the product 4–isopropyl–3–methyl–2,6–diphenylpyridine **247** (42.2 mg, 71%) was recovered as a spectroscopically clean yellow oil. Spectroscopic data for **247**: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 8.03 (dt, $^3J_{HH}$ = 7.0 Hz, $^2J_{HH}$ = 1.5 Hz, 2H, Ar<u>H</u>); 7.62 (s, 1H, H5); 7.56 (dt, $^3J_{HH}$ = 7.0 Hz, $^2J_{HH}$ = 1.5 Hz, 2H, Ar<u>H</u>); 7.47 (m, 6H); 3.29 (septet, $^3J_{HH}$ = 6.8 Hz, 1H, H7); 2.32 (s, 3H, H9); 1.35 (d, $^3J_{HH}$ = 6.8 Hz, 6H, H8,8'). **^{13}C {^{1}H} NMR** (125 MHz, $CDCl_3$, assignments confirmed by HMQC and HMBC spectra) δ 153.36; 132.99, 132.53; 129.86; 129.70; 129.57; 128.77; 128.67; 128.41; 128.29; 128.07; 125.06; 117.88; 30.20 (C7); 22.58 (C8,8'); 15.37 (C9). **HMQC** (500 MHz, $CDCl_3$, selected data only) δ 7.62 (H5) ↔ δ 117.88 (C5); δ 3.29 (H7) ↔ δ 30.20 (C7); δ 2.32 (H9) ↔ δ 15.37 (C9); δ 1.35 (H8,8') ↔ δ 22.58 (C8,8'). **HRMS** for $C_{21}H_{21}N$ requires *m/z* 287.16739, found *m/z* 287.16556; $C_{21}H_{20}N$ requires *m/z* 286.15958, found *m/z* 286.15883.

4–Benzyl–2,3,6–trimethylpyridine 248.

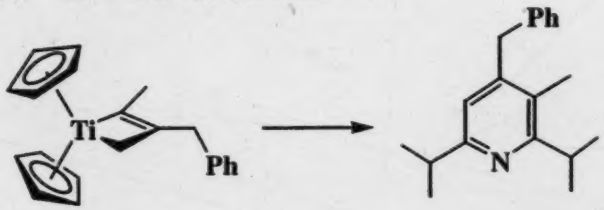


248

Following the general procedure described above, 1,1–bis(cyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene (25.0 mg, 0.077 mmol) and acetonitrile (48.0 mg, 1.16 mmol) were stirred at 80 °C for three hours during which time the red solution turned brown–red. Following column chromatography with neutral alumina (eluent: 10:1 CH_2Cl_2/MeOH), the product 4–benzyl–2,3,6–trimethylpyridine **248** was recovered as a spectroscopically clean yellow oil (8.4 mg, 51%). Spectroscopic data for **248**: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 7.26 (t, $^3J_{HH}$ = 6.9 Hz, 2H, ArH); 7.21 (t, $^3J_{HH}$ = 7.4 Hz, 1H, ArH); 7.09 (d, $^3J_{HH}$ = 7.4 Hz, 2H, H9); 6.74 (s, 1H, H5); 3.93 (s, 2H, H7); 2.49 (s, 3H, H12); 2.44 (s, 3H, H14); 2.13 (s, 3H, H13). **^{13}C {^{1}H} NMR** (75 MHz, $CDCl_3$) δ 156.40 (C2); 154.33 (C5); 147.68 (C4); 139.01 (C8); 128.68 (Ar); 128.54 (C3); 126.28; 122.39 (C5); 39.25 (C7); 23.92 (C14); 23.12 (C12); 14.40 (C13). **HMQC** (300 MHz, $CDCl_3$, selected data only) δ 7.26 (ArH) ↔ δ 128.54 (Ar); δ 7.21 (ArH) ↔ δ 126.28 (Ar); δ 7.09 (ArH) ↔ δ 128.68 (Ar); δ 6.74 (H5) ↔ δ 122.39 (C5); δ 3.93 (H7) ↔ δ 39.25 (C7); δ 2.49 (H12) ↔ δ 23.12 (C12); δ 2.44 (H14) ↔ δ 23.92 (C14); δ 2.13 (H13) ↔ δ 14.40 (C13). **HMBC** (300 MHz, $CDCl_3$, selected data only) δ 7.26 (ArH) ↔ δ 139.01, 128.68; δ 7.09 (H9) ↔ δ 128.68, 128.54, 39.25 (C7); δ 6.74 (H5) ↔ δ 128.54 (C3), 39.25 (C7), 23.92

(C14); δ 3.93 (H7) ↔ δ 147.68 (C4), 139.01 (C8), 128.68, 128.54 (C3), 126.28; δ 2.49 (H12) ↔ δ 156.40 (C2), 128.54 (C3); δ 2.44(H14) ↔ δ 154.33 (C5), 122.39 (C5); δ 2.13(H13) ↔ δ 156.40 (C2), 147.68 (C4), 128.54 (C3). **HRMS** for $C_{15}H_{17}N$ requires *m/z* 211.13609, found *m/z* 211.13582.

4–Benzyl–3–methyl–2,6–diisopropylpyridine 249.

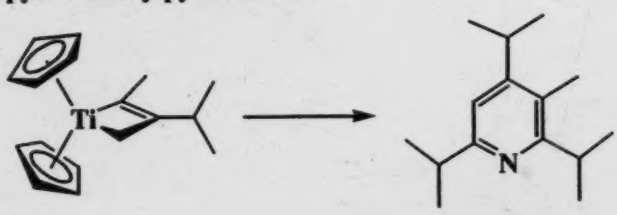


249

Following the general procedure described above, 1,1–bis(cyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene (50.0 mg, 0.16 mmol) and isobutyronitrile (161 mg, 2.32 mmol) were stirred at 80 °C for two hours during which time the red solution turned brown–red. Following column chromatography with neutral alumina (eluent: 10:1 CH_2Cl_2/MeOH), the product 4–benzyl–3–methyl–2,6–diisopropylpyridine **249** (43.5 mg, 53%) was recovered as a spectroscopically clean yellow oil. Spectroscopic data for **249**: **^{1}H NMR** (360 MHz, $CDCl_3$) δ 7.30 (t, $^3J_{HH}$ = 7.1 Hz, 2H, H10); 7.22 (t, $^3J_{HH}$ = 7.1 Hz, 1H, H11); 7.12 (d, $^3J_{HH}$ = 7.1 Hz, 2H, Ar<u>H</u>); 6.72 (s, 1H, H5); 3.97 (s, 2H, H7); 3.29 (septet, $^3J_{HH}$ = 6.9 Hz, 1H, H13); 2.95 (septet, $^3J_{HH}$ = 6.9 Hz, 1H, H15); 2.18 (s, 3H, H12); 1.27 (d, $^3J_{HH}$ = 6.9 Hz, 12H, H 14,14',16,16'). **^{13}C {^{1}H} NMR** (75 MHz, $CDCl_3$,

assignments confirmed by HMQC and HMBC spectra) δ 163.69 (C3); 163.26 (C6); 147.25 (C2); 139.41(C8); 128.71 (C9); 128.49 (C10); 126.15 (C11); 125.27 (C4); 119.12 (C5); 39.81 (C7); 35.82 (C15); 31.50 (C13); 22.60 (C14, 14', 16, 16'); 21.92 (C14, 14', 16, 16'); 13.52 (C12). **HMQC** (600 MHz, $CDCl_3$, selected data only) δ 7.30 (H10) ↔ δ 128.49 (C10); δ 7.22 (H11) ↔ δ 126.15 (C11); δ 7.12 (C9) ↔ δ 128.71 (C9); δ 6.72 (H5) ↔ δ 119.12 (C5); δ 3.97 (H7) ↔ δ 39.81 (C7); δ 3.29 (H13) ↔ δ 31.50 (C13); δ 2.95 (H15) ↔ δ 35.82 (C15); δ 2.18 (H12) ↔ δ 13.52 (C12); 1.27 (H 14,14',16,16') ↔ δ 22.60 (C 14,14',16,16'). **HMBC** (600 MHz, $CDCl_3$, selected data only) δ 7.12 (C9) ↔ δ 39.81 (C7); δ 6.72 (H5) ↔ δ 163.69 (C3), 125.27 (C4), 39.81 (C7), 35.82 (C15); δ 3.97 (H7) ↔ δ 147.25 (C2), 139.41 (C8), 125.27 (C4), 119.12 (C5), 39.81 (C7, self–correlation); δ 3.29 (H13) ↔ δ 163.69 (C3), 31.50 (C13, self–correlation), 22.60 (C 14,14'); δ 2.95 (H15) ↔ δ 163.26 (C6), 35.82 (C15, self–correlation), 22.60 (C 16,16'); δ 2.18 (H12) ↔ δ 163.69 (C3), 147.25 (C2), 125.27 (C4), 13.52 (C12, self–correlation). **HRMS** for $C_{19}H_{25}N$ requires *m/z* 267.19870, found *m/z* 267.19764.

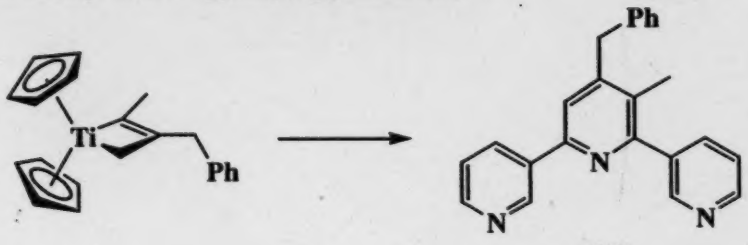
2,4,6–Trisisopropyl–3–methylpyridine 250.



250

Following the general procedure described above, 1,1–bis(cyclopentadienyl)–3–isopropyl–2–methyltitanacyclobutene (25.0 mg, 0.091 mmol) and isobutyronitrile (94.5 mg, 1.368 mmol) were stirred at 80 °C for six hours during which time the red solution turned brown. Following column chromatography with neutral alumina (eluent: CH_2Cl_2) the target material 2,4,6–trisisopropyl–3–methylpyridine **250** (4 mg, 20% yield) was recovered as a brown oil. Spectroscopic data for **250**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.81 (s, 1H, H5); 3.27 (septet, $^3J_{HH}$ = 6.7 Hz, 1H, H11); 3.13 (septet, $^3J_{HH}$ = 6.8 Hz, 1H, H9); 2.94 (septet, $^3J_{HH}$ = 6.9 Hz, 1H, H7); 2.23 (s, 3H, H13); 1.26 (d, $^3J_{HH}$ = 6.9 Hz, 6H, H12); 1.24 (d, $^3J_{HH}$ = 6.7 Hz, 6H, H8); 1.20 (d, $^3J_{HH}$ = 6.8 Hz, 6H, H10). **^{13}C {^{1}H} NMR** (75 MHz, $CDCl_3$) δ 163.20 (C2); 155.01 (C4); 123.78 (C3); 113.68 (C5); 108.59 (C6); 36.10 (C7); 31.66 (C11); 29.35 (C9); 22.67 (C10); 21.95 (C12); 13.12 (C13). **HMQC** (300 MHz, decoupled, $CDCl_3$, selected data only) δ 6.81 (H5) ↔ δ 113.68 (C5); δ 3.27 (H11) ↔ δ 31.66 (C11); δ 3.13 (H9)↔ δ 29.35 (C9); δ 2.94 (H7)↔ δ 36.10 (C7); δ 2.23 (H13) ↔ δ 13.12 (C13). **HMBC** (300 MHz, $CDCl_3$) δ 6.81 (H5) ↔ δ 123.78 (C3), 29.35 (C9); δ 3.27 (H11) ↔ δ 21.95 (C12); δ 3.13 (H9)↔ δ 155.01 (C4), 123.78 (C3), 22.67 (C10); δ 2.94 (H7)↔ δ 163.20 (C2); δ 2.23 (H13) ↔ δ 163.20 (C2), 155.01 (C4), 123.78 (C3); δ 1.24 (H8) ↔ δ 163.20 (C2), 36.10 (C7); δ 1.20 (H10)↔ δ 155.01 (C4), 29.35 (C9). **HRMS** for $C_{15}H_{25}N$ requires *m/z* 219.19870, found *m/z* 219.19821.

4–Benzyl–3–methyl–2,6–(3–pyridyl)–pyridine 251.



251

Following the general procedure described above, 1,1–bis(cyclopentadienyl)–3–benzyl–2–methyltitanacyclobutene (10.0 mg, 0.031 mmol) and 3–cyanopyridine (13.0 mg, 0.124 mmol) were stirred at 40 °C for five days during which time the red solution turned brown. Following column chromatography with neutral alumina (eluent: 10:1 CH_2Cl_2/MeOH) the target material, 4–benzyl–3–methyl–2,6–(3–pyridyl)–pyridine **251** was recovered as an impure brown oil (5 mg, 48%). Spectroscopic data for 4–benzyl–3–methyl–2,6–(3–pyridyl)–pyridine: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 9.17 (s, 1H); 8.84 (s, 1H); 8.66 (doublet of multiplets, J_{HH} = approx. 5 Hz, 1H); 8.62 (doublet of multiplets, J_{HH} = approx. 5 Hz, 1H); 8.33 (dt, $^3J_{HH}$ = 7.8 Hz, $^3J_{HH}$ = 1.9 Hz, 1H); 7.93 (dt, $^3J_{HH}$ = 7.9 Hz, $^3J_{HH}$ = 1.9 Hz, 1H); 7.50 (s, 1H, H5); 7.45–7.15 (m, 7H); 4.14 (s, 2H, H7); 2.32 (s, 3H, H12). **^{13}C {1H} NMR** (75 MHz, $CDCl_3$) δ 156.4; 152.0; 150.4; 150.3; 149.7; 149.0; 148.1; 137.9; 136.9; 136.6; 134.6; 134.3; 129.6; 128.9; 126.8; 123.5; 123.1; 120.7 (C5); 113.8; 112.5; 76.6; 39.7 (C7); 16.1 (C12). **HMQC** (300 MHz, $CDCl_3$, selected data only) δ 8.84 ↔ δ 150.4; δ 8.66 ↔ δ 149.0; δ 8.30 ↔ δ 134.3; δ 7.93 ↔ δ 136.9; δ 7.50 (H5) ↔δ 120.7 (C5); δ 4.14 (H7) ↔ δ 39.7 (C7); δ 2.32 (H12) ↔ δ 16.1 (C12).

HRMS parent *m/z* not detected. Parent *m/z* –H: for $C_{23}H_{18}N_3$ requires *m/z* 336.15009, found *m/z* 336.14928. For $C_{23}H_{17}N_3D$ requires *m/z* 337.15634, found *m/z* 337.15582. Electrospray mass spectrum for 1,1–bis(cyclopentadienyl)–5–benzyl–4–methyl–3,7–di(3–pyridyl)titana–2,6–diazacycloocta–2,4,7–triene (the double insertion titanacyclobutene complex precursor): **ES–MS** (positive ionization) for $C_{33}H_{31}N_4Ti$ requires: *m/z* (Ti isotope peaks at 529.2, 530.2, 531.2, 532.2, 533.2, 534.2). Found: (Ti isotope peaks at 529.2, 530.2, 531.2, 532.2, 533.2, 534.2).

viii. Conversion of titanacyclobutene complexes to phospha- and boracyclobutenes

3–Isopropyl–1,2–diphenyl–phosphacyclobutene 254.

254

To a solution of 1,1–bis(cyclopentadienyl)–3–isopropyl–2–phenyltitanacyclobutene (25.0 mg, 0.074 mmol) in toluene at –78 °C was added dichlorophenylphosphine (13.3 mg, 0.074 mmol). The solution was allowed to stand at –78 °C for three hours. In my hands, the small amount of the formed Cp_2TiCl_2 is not fully separated from the product by recrystallization, hence the yield of the reaction is not exactly available. However, by NMR spectroscopy the reaction appears to be quantitative. Spectroscopic data for

compound **254**: **^{1}H NMR** (360 MHz, C_6D_6, assignments confirmed by GCOSY, HMQC, HMBC spectra) δ 7.67 (m, 2H, 1–phenyl *ortho*); 7.40 (d, 2H, 2–phenyl *ortho*); 7.2–6.9 (m, 6H, ArH); 2.93 (septet, $^3J_{HH}$ = 6.8 Hz, 1H, H5); 2.53 (dd, $^2J_{HH}$ = 15.0 Hz, $^2J_{HP}$ = 9.4 Hz, 1H, H4); 1.86 (dd, $^2J_{HH}$ = 15.0 Hz, $^2J_{HP}$ = 4.3 Hz, 1H, H4'); 0.96 (d, $^3J_{HH}$ = 6.8 Hz, 3H, H6); 0.82 (d, $^3J_{HH}$ = 6.8 Hz, 3H, H6'). **^{13}C APT NMR** (75 MHz, C_6D_6, assignments confirmed by HMQC and HMBC spectra) δ 155.3 (d, $^2J_{CP}$ = 6.0 Hz, C3); 140.1 (d, $^1J_{CP}$ = 34.4 Hz, C2); 139.5 (d, $^1J_{CP}$ = 33.8 Hz, 1–phenyl *ipso*); 136.4 (d, $^2J_{CP}$ = 10.5 Hz, 2–phenyl *ipso*); 132.1 (d, $^2J_{CP}$ = 18.8 Hz, 1–phenyl *ortho*); 129.4; 128.7 (d, $^3J_{CP}$ = 5.0 Hz, 1–phenyl *meta*); 127.54 (d, $^3J_{CP}$ = 5.7 Hz, 2–phenyl *ortho*); 127.2; 30.5 (d, $^3J_{CP}$ = 2.5 Hz, C5); 24.2 (d, $^1J_{CP}$ = 8.2 Hz, C4); 20.7 (C6); 19.7 (C6'). **HMQC** (300 MHz, decoupled, C_6D_6, selected data only) δ 7.67 (1–phenyl *ortho*) ↔ δ 132.1 (1–phenyl *ortho*); δ 2.93 (H5) ↔ δ 130.5 (C5); δ 2.53 (H4) ↔ δ 24.2 (C4); δ 1.86 (H4') ↔ δ 24.2 (C4); δ 0.96 (H6) ↔ δ 20.7 (C6); δ 0.82 (H6') ↔ δ 19.7 (C6'). **HMBC** (300 MHz, C_6D_6, selected data only) δ 7.40 (2–phenyl *ortho*) ↔ δ 140.1 (C2); δ 2.93 (H5) ↔ δ 155.3 (C3), 140.1 (C2), 24.2 (C4), 20.7 (C6), 19.7 (C6); δ 2.53 (H4) ↔ δ 155.3 (C3), 140.1 (C2); δ 1.86 (H4') ↔ δ 155.3 (C3), 140.1 (C2); δ 0.96 ↔ δ 155.3 (C3), 140.1 (C2), 30.5 (C5), 19.7 (C6'); δ 0.82 ↔ δ 155.3 (C3), 140.1 (C2), 30.5 (C5), 20.7 (C6). **^{31}P {^{1}H, CPD}** (81 MHz, C_6D_6) δ –14.82. **HRMS** $C_{18}H_{19}P$ requires *m/z* 266.12244, found 266.12247.

1,2–Diphenyl–3–isopropylboracyclobutene 261.

261

To a solution of 1,1–bis(cyclopentadienyl)–3–isopropyl–2–phenyltitanacyclobutene (50.0 mg, 0.148 mmol) in toluene at –35 °C was added dichlorophenylborane (23.6 mg, 0.148 mmol). The solution was allowed to stand at –35 °C for 16 hours. The solvent was removed *in vacuo* and the residue triturated with cold (–35 °C) hexane. This solution was allowed to stand overnight at –35 °C during which time a orange precipitate formed which was the product, 1,2–diphenyl–3–isopropylboracyclobutene **261** and a small amount of the by–product Cp_2TiCl_2. The small amount of the formed Cp_2TiCl_2 is not fully separated from the product by recrystallization, hence the yield of the reaction is not exactly available. However, by NMR spectroscopy the reaction appears to be quantitative. Spectroscopic data for compound **261**: **^{1}H NMR** (360 MHz, C_6D_6, assignments confirmed by gHSQC, HMQC, HMBC spectra) δ 7.75 (broad singlet, 2H); 7.23 (broad singlet, 2H); 7.20–7.05 (m, 5H, ArH); 6.97 (t, $^3J_{HH}$ = 7.4 Hz, 1H); 3.25 (septet, $^3J_{HH}$ = 6.8 Hz, 1H, H5); 2.57 (broad singlet, 2H, H4); 1.05 (d, $^3J_{HH}$ = 6.8 Hz, 6H, H6). **^{13}C {1H} NMR** (75 MHz, C_6D_6, assignments confirmed by HMQC and HMBC spectra) δ 143.7; 142.5 (C2); 141.2; 136.7; 132.4; 129.7; 128.4; 127.8; 125.9; 119.5; 31.8 (C5); 29.7 (C4); 21.7 (C6). **gHSQC** (600MHz, C_6D_6, selected correlations only) δ 7.75

↔ δ 136.78; δ 7.23 ↔ δ 129.79; 7.1 ↔ δ 132.42; δ 6.97 ↔ δ 128.48; δ 3.25 (H5) ↔ δ 31.89 (C5); δ 2.57 (H4)↔ δ 29.70 (H4); δ 1.05 (H6) ↔ δ 21.76 (H6). **HMBC** (600 MHz, selected correlations only) δ 7.05 ↔ δ 142.52; δ 7.02 ↔ δ 141.25 (Ar *ipso*); δ 6.97 ↔ δ 129.79; δ 3.25 ↔ δ 142.52 (C2), 29.70 (C4), 21.76 (C6); δ 2.57 (H4) ↔ δ 142.52 (C2), 31.89 (C5); δ 1.05 ↔ δ 31.89 (C5), 21.76 (C6). ^{11}**B** {^{1}**H**} (64 MHz, C_6D_6) δ 69.96. **HRMS** $C_{18}H_{19}OB$ requires *m/z* 262.15289, found 262.15252.

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